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GRANT NUMBER DAMD17-96-1-6227

TITLE: Dietary Intake, Alcohol Consumption, and Menopausal Status: A Comparison of Hispanic and Non-Hispanic White Women

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REPORT DATE: September 1999

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

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DTIC QUALITY INSPECTED 4

20000828 220

REPORT DOCUMENTATION PAGE

Form Approved
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Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	September 1999	Annual (1 Sep 98 - 31 Aug 99)

4. TITLE AND SUBTITLE
Dietary Intake, Alcohol Consumption, and Menopausal Status: A Comparison of Hispanic and Non-Hispanic White Women

5. FUNDING NUMBERS
DAMD17-96-1-6227

6. AUTHOR(S)
Kathy Baumgartner

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The University of Texas Health
Science Center at Houston
Houston, Texas 77225

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200*

The third year of work towards the completion of a doctoral degree, focused on breast cancer epidemiology, at the University of Texas School of Public Health, Houston, Texas has been completed. Analyzed data are a subset of that collected for the study, 'Breast Cancer Epidemiology in NM Hispanic Women'. The Principal Investigator of this training grant served as Project Director of this study conducted by the Epidemiology and Cancer Control Program at the University of New Mexico. The New Mexico Tumor Registry ascertained cases (n=712) newly diagnosed with breast cancer (1992 - 1994) aged 30-74 years. Controls(n=844) were identified by random digit dialing and were frequency-matched for ethnicity, age-group, and health planning district. In-person interviews were conducted, and data collected for breast cancer risk factors, including alcohol intake. The doctoral dissertation focused on alcohol as a risk factor for Hispanic and non-Hispanic white women, adjusting for potential confounders. 'Past' alcohol consumption, based on history of alcohol intake at ages 25, 35, and 50, and 'recent' intake based on a food frequency questionnaire were investigated. Hormone receptor status was also investigated.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Breast Cancer, alcohol, hormone receptor status, menopausal status, Hispanic ethnicity, case-control study	160
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

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Kathy B. Baumgartner 9/27/99

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INTRODUCTION

The focus of this predoctoral fellowship training grant, *"Dietary Intake, Alcohol Consumption, and Menopausal Status: A Comparison of Hispanic and non-Hispanic Women"* and doctoral dissertation, is on alcohol and its association with other risk factors for breast cancer. The basic hypothesis is that alcohol, based on evidence from other studies, may be important in the increasing rates of breast cancer. The third year of grant work on the predoctoral fellowship training grant focused on data analyses and interacting with the doctoral dissertation committee to complete the final dissertation in compliance with the requirements of the University of Texas School of Public Health, Houston, Texas (UTSPH). The scope of the dissertation was narrowed to alcohol consumption, excluding diet in general, based on the recommendation of the doctoral thesis committee. However, total energy intake and total fat were evaluated as potential confounders. Much of this report is drawn from the dissertation, but the present report includes additional details and tables. The final dissertation submitted to UTSPH and formally accepted in May 1999 is provided in Appendix I.

The following report details: the significance of this research and the specific aims and hypotheses; a background review of previous studies on alcohol consumption and breast cancer including, hormone receptor status of breast tumors, and studies of Hispanic ethnicity and breast cancer risk; materials and methods, including selection of cases and controls, and data collection; statistical methods, including the measurement of alcohol exposure variables, hormone receptor status, confounding variables, and data analysis; results; key research accomplishments; reportable outcomes; and conclusions.

The incidence of breast cancer in Hispanic women has been documented to be lower than in non-Hispanic white women residing in the West and Southwest (1, 2). In New Mexico, incidence and mortality rates have increased rapidly among Hispanic women since the late 1950s, especially in the younger age-groups, although prevalence rates for Hispanic women are intermediate to those for American Indians and non-Hispanic white women (1-4). Incidence rates increased by 56% over a 19-year period, and mortality increased by almost 100% over the 30-year period 1958-1987 (3). Incidence rates reported for Hispanic women *vs.* non-Hispanic white women range from 58/100,000 *vs.* 112/100,000 for the time-period 1983 to 1987 in New

Mexico (3), to 69.8 *vs.* 115.7 for the time-period 1988 to 1992 for Surveillance, Epidemiology and End Results (SEER) data (5).

The proposed study provided an opportunity to further research on the primary cancer for Hispanic women (6). It is projected that Hispanics will represent the largest ethnic group in the US population by the year 2000, and account for approximately 17% of the total U.S. population by the year 2030 (7). New Mexico has the largest percentage of Hispanics (40%) to total state population in the United States (7), and has a statewide cancer registry, the New Mexico Tumor Registry (NMTR), as a part of the SEER Program of the National Cancer Institute. The SEER registries cover approximately 14% of the US population. This includes 25% of the Hispanic population. The majority of the Hispanic population in the SEER coverage area resides in Los Angeles (60%), New Mexico (10%), San Francisco and San Jose/Monterey (9%), and Connecticut (4%) (5).

Although breast cancer incidence rates and mortality rates have increased among Hispanic women, the causes of breast cancer in this minority population have not been adequately characterized. There are few data available on breast cancer risk factors for Hispanic women (3, 4, 8-10), and in particular, insufficient understanding of dietary and alcohol practices (11). New Mexican Hispanic women, especially over age 50, are reported to have lower alcohol intake, and are more likely to be non-drinkers than non-Hispanic white women (12). One study has reported that alcohol intake was associated with a nonsignificant increased breast cancer risk for Hispanic women (13). Otherwise, the association of alcohol consumption with breast cancer risk has not been investigated in Hispanic women.

The purpose of this study was to evaluate the primary hypothesis that alcohol consumption is associated with increased breast cancer risk among Hispanic and non-Hispanic white women using data from a statewide population-based case-control study, the 'New Mexico Women's Health Study' (NMWHS). The NMWHS, was initiated in 1992 to investigate etiologic risk factors for breast cancer among Hispanic and non-Hispanic white women. These data were used for this dissertation research to investigate three hypotheses by menopausal status: 1) alcohol consumption is associated with an increased breast cancer risk among Hispanic and non-Hispanic white women; 2) this risk is higher in Hispanics than non-Hispanic whites; and, 3) alcohol intake is associated with an increased risk for hormone-receptor negative breast cancer.

SPECIFIC AIMS

In order to investigate these hypotheses the specific aims were.

1. To estimate the risk of breast cancer for Hispanic and non-Hispanic white women who consume alcohol.

The weight of evidence has consistently shown an increased risk of breast cancer with alcohol consumption, defined by both a modest and high intake, among both pre- and postmenopausal women (14-16). Risk has been on the order of a 30% to 70% increase. Alcohol consumption as a main effect was evaluated in terms of both recent and past intake, in addition to lifetime exposure. All three measures have been reported to increase risk of breast cancer (13, 14, 16, 17), although overall, the evidence suggests that alcohol may be more important as a late-stage promoter for breast cancer risk, suggesting a stronger contribution to risk from recent intake (14, 16, 18).

Studies have primarily included non-Hispanic white women. Only one study of alcohol consumption and breast cancer risk has included Hispanic ethnicity as a risk factor (13). Results for average lifetime alcohol intake indicated a 24% (0.70-2.19) increase in risk per 13 grams(g)/day. This study was limited to postmenopausal women in Los Angeles, and the sample size by ethnicity was not included.

2. To estimate the risk of hormone receptor breast cancer for Hispanic and non-Hispanic white women for alcohol consumption.

Hormone receptor status appears to be related to prognosis and survival, and possibly to etiology (19, 20). It has offered an additional insight into associations of certain risk factors (i.e. alcohol, dietary fat, parity, body mass index) with breast cancer (21-24). Some studies (21-23) have shown an association between alcohol consumption and hormone receptor status, variously defined as a single estrogen receptor (ER) measure, progesterone (PR) measure, and the joint combination of ER/PR status. In the cohort 'Iowa Women's Health Study', an increase in risk for ER-/PR- breast tumors was reported for postmenopausal women for 'ever' use of alcohol (RR=1.37, 95%CI 0.86-2.18) (23). This risk increased for women who were in the highest alcohol intake group, and also on estrogen replacement therapy, or had a family history of breast cancer, or who were obese (22). In contrast, a case-control study of Japanese women, aged 25 years and older, failed to find an association between alcohol consumption and joint hormone

receptor status (25). However, alcohol exposure was measured dichotomously as 'ever' *vs.* 'never' use, and only 40% of cases had known receptor status.

To date, there are no studies investigating the presence of a differential risk for hormone receptor breast cancer subtypes and alcohol consumption by ethnicity. Results, based on the large 'Patient Care Evaluation Studies of Breast Cancer' investigation of women 20 to 79 years of age, showed no difference between Hispanic and non-Hispanic white ethnicity for ER/PR status, when ER+PR+ breast cancer cases were compared with ER+PR-, ER-PR+, or ER-PR- cases (26). However, this was a case-case breast cancer study, and the analysis included only 236 Hispanic women out of a total of 410.

BACKGROUND - PREVIOUS STUDIES

Alcohol consumption

Alcohol consumption is a common exposure. The National Center for Health Statistics (27) provides figures reporting that 61% of women over the age of 18 are current consumers of alcohol (12 or more drinks per year). Of these women, 39% reported their usage as light (≤ 3 drinks/week), 27% as moderate (4-13 drinks/week), and 9% as heavy (14+ drinks/week). Alcohol, as an important component of dietary intake, is subject to modification more easily than the established reproductive risk factors. The following figures of alcohol consumption from selected studies provide estimates of the prevalence of alcohol consumption among women with breast cancer compared to those without breast cancer.

Percent ever drinkers reported in several case-control studies

	Cases	Controls
Toniolo et al. (1989) (28)/Italy	72	63
	[15]	[7.4]
Rosenberg et al. (1990) (29)/US	70	74
Howe et al. (1991) (30)/US	67	69
	[5]	[3.6]
Friedenreich et al.(1993) (31)/Canada	77	76
	[8]	[6.8]
Swanson et al. (1997) (14)/US	65	62
Longnecker et al. (1995) (16)/US	85	83
	[8]	[5]

[ ] percent associated with heavy drinkers, variously defined in different studies

There are more than 50 ecological, case-control, and cohort studies examining the association of alcohol and breast cancer (32). The majority have reported consistent evidence for a positive association between breast cancer and alcohol intake (32). Case-control studies have provided the strongest evidence for an association between alcohol consumption and breast cancer. Rosenberg (17) gives a succinct review of the 18 studies reported in the literature from 1982 through 1992 focused primarily on recent drinking. Studies were included if there were at least 200 prevalent cases with sufficient data on methodology and participation rates no lower than 60%. Results from one study showed an inverse association and odds ratios (ORs) for four studies were reported to be close to the null (< 1.2), whereas eight of the 13 studies with positive associations were reported to have ORs greater than the null, but $\leq$ 1.8. In the remaining four positive studies, it was reported that at least one odds ratio was above 1.8. These were hospital-based studies conducted in France (Odds Ratio (OR)=3.5 for >17 drinks/week), and Italy (OR=2.2 for >3 drinks/day; OR=2.2 for >24.35 g/day; OR=2.4 for < 0.5 liters/day) (17). Estimates reported from population-based studies have ranged from 1.2 to 1.7, but these studies have had lower participation rates (60% to 80%) than the hospital-based studies. In these studies, stratification was not always made on the basis of menopausal status, a possible effect modifier of the association between alcohol consumption and risk of breast cancer. Associations were noted with past alcohol intake prior to age 30, but estimates for dose-response were inconsistent.

Some studies showed an increased risk for those who consumed as little as one drink per day, while other studies reported an increased risk of breast cancer for those consuming only high levels of alcohol (17).

The eight cohort studies of breast cancer reviewed by Rosenberg ranged in follow-up time from 4 to 30 years, and were conducted in the U.S. (17). At least two suffered from high loss-to-follow-up rates. Results showed the following associations: null - 1; positive - 8. Overall relative risk estimates for studies ranged from 1.2 to 3.3. In the four studies with the majority of cases, the relative risk for breast cancer did not exceed 1.6, and was associated with an intake of at least 15+ g/day (about 1 drink) of alcohol (17).

The recent studies by Longnecker et al. (15, 16, 33) and Swanson et al. (14) have built on the previous investigations, and many of their results are detailed below. The following provides a discussion of results for ever *vs.* never lifetime alcohol consumption, recent *vs.* past alcohol intake, dose-response, beverage type, the association of alcohol and hormone levels in studies of human female subjects, as well as animal studies.

Ever *vs.* never and lifetime alcohol consumption

Longnecker et al.'s meta-analysis of 12 case-control studies resulted in an odds ratio of 1.4 (95% Confidence Interval (95%CI) 1.0-1.8) for consumption of 24 g/day of alcohol (2 drinks) and risk of breast cancer. Results, based on four cohort studies, indicate a relative risk of 1.7 (95%CI 1.4-2.2) associated with consumption of 24 g/day of alcohol (33). Based on six of the case-control studies, the risk of breast cancer associated with 'ever' alcohol consumption was increased by only 10% (OR=1.1, 95%CI 1.0-1.2). This attenuation is probably due to the fact that the majority of women were light to moderate drinkers (33).

In their case-control study, based on 15,825 subjects from four states, Longnecker et al. (16) ascertained pre- and postmenopausal incident breast cancer cases <75 years of age who were diagnosed from 1988 through 1991, and reported to statewide cancer registries. A telephone questionnaire was used to assess alcohol intake of beer, wine, and liquor during five periods of life (16-19, 20-29, 30-39, 40-59, 60-74 years). Controls were drawn from two different sources and frequency-matched by age-group. Average lifetime alcohol consumption was based on the period from 16 years of age through the previous age interval. Lifetime average consumption for 13 g/day compared with lifelong abstainers was associated with a 31% increase in risk of breast

cancer (95%CI 1.20-1.43), and a statistically significant trend across categories of alcohol consumption.

The recently reported case-control study by Swanson et al. (14), was based on 1,645 premenopausal incident breast cancer cases diagnosed during 1990-1992 in women 20 to 44 years of age, and frequency-matched to controls for age and study site. The odds ratio for women defined as ever drinkers compared with nondrinkers was 1.1 (95%CI 1.0-1.3). A primary focus of this study was the effect of recent *vs.* usual alcohol intake by level of consumption, since previous studies had noted indirect evidence for the importance of recent alcohol intake. They evaluated alcohol usage patterns, exposure periods reflecting the teens, twenties, and thirties, beverage type, and stage of disease.

Recent *vs.* past alcohol consumption

Longnecker et al. (16) and Swanson et al.'s (14) investigations have shown a stronger association between 'recent' alcohol consumption and increased risk of breast cancer compared with 'past' alcohol intake. In Longnecker et al.'s case-control study, 'recent' alcohol consumption was defined as intake in the previous age interval prior to the reference date, and 'past' alcohol consumption as intake prior to 30 years of age. Results indicated that 'recent' *vs.* 'past' alcohol consumption appeared to be more strongly associated with risk of breast cancer (OR=1.21 for 13 g/day alcohol, 95%CI 1.09-1.34 *vs.* OR=1.09 for 13 g/day alcohol, 95%CI 0.95-1.24). Swanson et al. reported a 70% increase in risk of breast cancer associated with 'recent' alcohol consumption (OR=1.70, 95%CI 1.2-2.5), although this was restricted to women consuming $\geq$14 drinks/week (14). 'Past' alcohol consumption was based on the average intake for women during their teens, twenties, and thirties (14). Results by level of alcohol intake for the three age-period exposures indicated that risk increased 34% (95%CI 0.7-2.6) in the teen years for consumption of $\geq$7 drinks per week, 29% (95%CI 0.9-2.0) in the twenties for consumption of $\geq$14 drinks per week, and 80% (95%CI 1.2-2.6) in the thirties for consumption of $\geq$14 drinks per week.

Dose-response relationship

The strongest evidence for a dose-response relationship of alcohol consumption and the risk of breast cancer comes from Longnecker et al.'s 1995 large, case-control study (16). Risk of breast cancer showed a monotonic increase by alcohol intake for all subjects combined with the

exception of the highest category of alcohol intake (OR=1.75, 95%CI 1.16-2.64 for 46+ g/day alcohol). Results ranged from an odds ratio of 1.13 (95%CI 1.01-1.26) for 0-5 g/day alcohol, to 2.30 (95%CI 1.51-3.51) for 33-45 g/day alcohol, adjusted for age, state, age at first full term pregnancy, parity, body mass index (BMI), age at menarche, education, benign breast disease, and family history of breast cancer (16). The risk estimate based on a continuous measure of the lifetime average number of grams of alcohol consumed daily was 1.31 (95%CI 1.20-1.43, P for trend <.0001) for 13 g/day (approximately 1 drink).

Swanson et al. (14), found an increased risk for breast cancer at a high dose (14+ drinks/wk) (OR=1.7, 95%CI 1.2-2.5), but no clear dose-response or gradient across categories of alcohol intake, adjusted for ethnicity, oral contraceptive use and parity. Howe et al.'s study also suggested a possible 'threshold' effect based on a pooled analysis of six case-control studies (34). A significant increase in risk was seen for women consuming 40 g/day or more of alcohol (OR=1.6 (95%CI 1.19-2.40), adjusted for total energy, fat, fiber, and vitamin C. The possibility of a threshold effect would require levels of alcohol intake to be high in order to detect an association. In Longnecker et al.'s case-control study (16), risk was higher, although not statistically significant, for postmenopausal women compared with premenopausal women as noted below.

Odds Ratios (OR) and 95% confidence intervals (CI) for average lifetime alcohol consumption, stratified by menopausal status, based on a population-based case-control study in Maine, Massachusetts, New Hampshire and Wisconsin (1988-1991)

Average alcohol consumption g/day	Premenopausal OR (95%CI)	Postmenopausal OR (95%CI)
0	1.00	1.00
>0-5	1.25 (0.97-1.61)	1.05 (0.94-1.17)
6-11	1.25 (0.93-1.67)	1.07 (0.92-1.24)
12-18	1.18 (0.83-1.67)	1.20 (1.00-1.44)
19-32	1.43 (0.96-2.13)	1.59 (1.28-1.98)
33-45	1.65 (0.88-3.10)	2.01 (1.37-2.95)
≥46	1.61 (0.90-2.86)	2.28 (1.51-3.44)
13 g/day	1.18 (1.03-1.36) P for trend = .02	1.27 (1.16-1.39) P for trend <.001

Longnecker et al. 1995:925 (16)

Beverage type

The pattern of risk by beverage type (wine, beer, hard liquor) has not always been consistent, and studies have varied as to which beverage, if any, carries the highest risk (35). This issue is a hard one to disentangle due to the mixture of beverages that tends to occur with alcohol consumption. Swanson et al.'s (14) study reported the strongest risk for beer consumption (OR=2.6, 95%CI=1.4-4.8) compared with wine and liquor intake; whereas Longnecker et al.'s (16) study showed an increased risk for both beer (OR=1.25, 95%CI=1.13-1.39) and liquor (OR=1.18, 95%CI=1.07-1.31). Mutual adjustment for beverage type in the study by van den Brandt et al. (36) suggested that the association was present for wine (OR=1.50, 95%CI 0.63-3.57), and liquor (OR=1.67, 95%CI 0.82-3.39), but not for beer consumption (OR=0.95, 95%CI 0.61-1.48). However, associations reported for one beverage *vs.* another may merely reflect the dominant beverage consumed by the heaviest drinkers (35). Although some studies have shown a difference in risk by beverage type, risk has not been consistently associated with one type, implying that risk is associated with alcohol intake in general, and not with any other specific component (18).

Association of alcohol and hormone levels

A small clinical trial has proposed a possible mechanism for the positive association between alcohol consumption and breast cancer, with the detection of a statistically significant increase in plasma and urinary hormones (37). A group of 34 premenopausal women, aged 20-40 years, was enrolled in a controlled-diet study for six consecutive months. Subjects served as their own controls to reduce interindividual variation. Following exposure to 30 g/day of ethanol for three menstrual cycles, they abstained from alcohol for the remaining three cycles. Results showed elevated serum levels of total and bioavailable estrogen (37). An increase in plasma estradiol levels has been shown to also increase three-fold in postmenopausal women following a single dose of 0.7 grams(g)/kilogram (kg) alcohol (38).

The link of alcohol with estrogen level provides a rational mechanism between alcohol intake and breast cancer, implying an effect on estrogen production and metabolism. Estrogen and progesterone are required for the cyclic proliferation of mammary ductal cells during the menstrual cycle and for lobuloalveolar growth during pregnancy. Hormonal level is hypothesized to be important in the etiology of breast cancer by increasing breast epithelial cell

division during relevant developmental periods, and enhancing the possibility of carcinogenesis (39). Studies in the 1970s established increased plasma estrogen and estradiol levels in postmenopausal women with breast cancer (40), supporting the hypothesis that breast neoplasia is the result of excessive hormonal stimulation.

Results based on experimental animal models of alcohol exposure and breast cancer are inconsistent (41-43). These studies, however, are difficult to conduct, because there are few good animal models of spontaneous breast cancer. Most studies are conducted using rodents. Dogs are a better model because they develop natural spontaneous breast tumors, but are considered too expensive for most studies (41). The majority of animal studies have reported no evidence for an association between alcohol and mammary carcinogenesis (42). McDermott et al. (42) conducted an experiment in which female Sprague-Dawley rats given an established carcinogen were randomly assigned to dietary ethanol (4.4g/kg/day) or placebo. The incidence of tumors was significantly lower in the ethanol than control group ($p < 0.001$), and there was no statistically significant difference between groups in mean number of tumors, tumor growth rate, or time of appearance to first tumor. Endocrine levels were not measured for the two groups. Positive results have shown that ethanol consumption >20% of calories decreased serum progesterone and mammary gland maturation and differentiation resulting in an increase in the density of carcinogen sensitive histological structures (44, 45). These changes might increase susceptibility to breast cancer carcinogens, but would not necessarily cause cancer. It has been suggested that progesterone when co-occurring with estrogen may further increase mitotic activity in breast epithelium (46).

Reasons cited for the inconsistent or negative results from animal studies include mode of ethanol administration (gavage, drinking water, liquid diet), and amount of ethanol administered which has usually been 20% or more of total calories with no evaluation of lower doses (43). These factors are thought to have an effect on the rate of ethanol absorption, level and duration of ethanol, and blood-level metabolites, all of which might subsequently affect metabolism (43). Ethanol administered as part of a natural product diet *vs.* a liquid diet may also result in tumor response variation (43).

Hormone-receptor status of breast tumors

Hormone-receptor status has received attention as a means of identifying subtypes of breast cancer that are not only related to prognosis and survival, but possibly to separate risk factors for breast cancer (19, 20). Estrogen receptor protein binds and transfers estrogen to the nucleus of a cell, and is found in about 60% of breast cancers (47). The number of estrogen receptors in breast cancer cells is associated with cell differentiation, with tumor response to antiestrogen or tamoxifen therapy, and to oophorectomy (48). Receptor-positive tumors are reported to occur more frequently among postmenopausal women than among premenopausal women (47). Patients with both ER+/PR+ status are characterized by the highest response rates (approximately 70%) to endocrine therapy, whereas those with ER-/PR- tumors (approximately 10%) show the poorest response, and those with discordant status (30-40%) show an intermediate response (48-50)

Several studies have demonstrated an association of alcohol consumption with hormone-receptor status, although analyses and results have varied by use of separate subtypes, ER or PR status, (21), or the joint combination of ER/PR status (22, 23). Risk factors for breast cancer, including family history of breast cancer (51), BMI (52), dietary fat (24, 53), parity, age at first birth, age at menarche, and body fat distribution (23) have shown different patterns by hormone-receptor status. These results may suggest different etiologies associated with disease heterogeneity or separate hormone-receptor subtypes. Based on data from a case-control study conducted in New York (1982-1984) of 1,152 women, aged 20-79 years of age, Nasca et al. reported an odds ratio of 1.18 (95%CI 0.88-1.57) for <1.5 g/day alcohol with an increase to 1.35 (95%CI 0.99-1.85) for ≥15.0 g/day alcohol associated with ER+ breast tumors (21). Breast cancer cases with ER+ status were more likely to be ≥65 years (64%) compared with ER- cases (54%), to have reported the cessation of menstruation (77% *vs.* 68%), and to have a greater duration (14+ years) of cigarette smoking (37% *vs.* 30%), following adjustment for covariates.

Data from the cohort, 'Iowa Women's Health Study', based on 610 women with a joint ER/PR status and aged 55-69 years, showed an association between PR+ status and risk factors which measure endogenous hormone exposure (23). However, alcohol use within the last year was found to increase the risk for ER-/PR- breast tumors in both stratified (RR=1.55 (95%CI 1.00-2.41), and polychotomous logistic regression analyses (RR=1.37 (95%CI 0.86-2.18).

Gapstur et al. (22) extended analyses of the 'Iowa Women's Health Study' to evaluate the risk of breast cancer hormone-receptor status and the presence of interaction between alcohol consumption (0, <4.0, ≥4.0 g/day) with three other risk factors. ER-/PR+ was excluded due to small sample size. Relative risks by hormone-receptor status (ER+/PR+, ER+/PR-, ER-/PR-) for those on estrogen replacement therapy were reported to be 1.8 (95%CI 1.3-2.5), 1.3 (95%CI 0.6-2.5), and 2.6 (95%CI 1.4-4.9) respectively, at the highest alcohol intake of ≥4.0 g/day. Results for family history were 1.7 (95%CI 1.2-2.5), 0.8 (95%CI 0.3-2.3), and 3.1 (95%CI 1.6-6.2) for women with any level of alcohol intake, and results for the highest quintile of BMI >30.70 were 0.9 (95%CI 0.5-1.9), 1.8 (95%CI 0.7-4.7), and 2.0 (95%CI 0.7-5.6) for 'drinkers' (22)

In contrast to these results, the initial analyses of the association between alcohol consumption and breast cancer for the 'Iowa Women's Health Study' showed only an age-adjusted relative risk of 1.28 (95%CI 0.93-1.76). This risk increased (RR = 1.46, 95%CI 1.04-2.04; P for trend=0.04, for the highest alcohol intake of 15+ g/day) with adjustment for covariates (BMI, age at first livebirth, age at menarche, and family history of breast cancer) (54). Significant multiplicative interaction was detected between alcohol intake and noncontraceptive estrogen use for the two highest levels of alcohol intake (RR=1.88, 95%CI 1.30-2.72 for 5.0-14.9 g/day; RR=1.83, 95%CI 1.18-2.85 for 15+ g/day), whereas there was no association between alcohol and breast cancer detected among never-users of estrogen (54).

The association of ethnicity with hormone-receptor status was examined for 13,239 breast cancer cases in the 'Patient Care Evaluation Study of Breast Cancer', ascertained during 1990 (26). The status group ER+/PR+ was used as the referent group in the polychotomous logistic regression analysis which did not show a significant difference for ER/PR status for Hispanic *vs.* non-Hispanic white women: ER+PR-, OR=0.88 (95%CI 0.65-1.21); ER-PR+, OR=1.20 (95%.CI 0.83-1.75); and ER-PR-, OR=0.95 (95%CI 0.74-1.23). However, this may be due to the lack of a true nondiseased control group.

Studies of Hispanic ethnicity and breast cancer risk

Studies have shown that incidence and mortality rates for other chronic diseases such as diabetes and heart disease show a different pattern for Hispanics compared with non-Hispanic whites in New Mexico (55). The majority (75%) of Hispanics residing in New Mexico are primarily lifelong residents, compared with only 15% of non-Hispanic white women.

Additionally, for many, their families have lived here for several generations, and are composed of descendants of Spanish colonists of the 16th, 17th, and 18th centuries who intermarried with Pueblo Indians and recent Mexican immigrants. Thus, they are not strictly comparable to other Hispanic groups such as Mexican-Americans who are recent immigrants to the United States. However, the Hispanic population in the U.S. is characterized by a diversity across a spectrum of factors, including background nationality, ethnicity, socioeconomic status, culture, and religion (7).

There are few published studies comparing Hispanic women with other ethnic groups for breast cancer. Two studies conducted in Texas reported a lower incidence of familial breast cancer among Hispanic women compared with Blacks and non-Hispanic whites (8), and the suggestion of an increased risk of mortality due to breast cancer with increased age at first child-birth (4). Hispanic women, over the period 1980 to 1992, were reported to have more late stage breast cancer than non-Hispanic white women (37% *vs.* 28%), and to be less than 50 years old at age of diagnosis (44% *vs.* 28%) (56). In contrast, based on SEER data, Hispanic women were reported to present at an earlier stage of diagnosis for the time-period 1983-1992 compared with 1973-1982. However, although detection now occurs more frequently at the local stage, survival has not improved (57). In an analysis of the 148 Hispanic cases and 167 controls (43% based on New Mexico Hispanics) drawn from 'The Cancer and Steroid Hormone Study (CASH)', a statistically significant increased risk for breast cancer was found for women who reported having a mother or sister with a history of breast cancer (OR=1.89) (9). Although not statistically significant, the expected pattern for number of full-term pregnancies, age at first full-term birth (FFTB), and benign breast disease were found, but not for early age at menarche.

Latino ethnicity was found to be a significant predictor of dietary and alcohol intake after adjustment for relevant covariates in a study of California Latino dietary practices (11). Latinos compared with non-Latino whites were less likely to have had liquor in the past month (OR=0.6). Less acculturated (greater use of Spanish language) Latinos compared with highly acculturated (greater use of English) Latinos reported less alcohol consumption in the past month (OR=0.7). Postmenopausal Hispanic women in New Mexico, compared with non-Hispanic whites, are reported to have a similar intake of beer, but less intake for wine and liquor (58) and overall, alcohol consumption is lower.

Elledge et al. reported that Hispanic women had worse overall 5-year survival compared with non-Hispanic white women (65% *vs.* 75%), and differed for tumor biologic factors (59). Significant differences, based on the Hispanic *vs.* non-Hispanic white comparison, were present for age (61% *vs.* 76%), tumor size (32% *vs.* 45%), and nodal status (30% *vs.* 21%). Age was found to modify the association between ethnicity and hormone-receptor status. Hispanic women were intermediate to non-Hispanic whites and Blacks for ER+ status tumors for ages 35 to 50 years, (P for difference <0.12), and for 50 years or greater (P for difference <0.002). This was also true for PR+ status for women 50 years of age or older (P for difference <0.006) (59).

Only one study of alcohol consumption and breast cancer risk has included Hispanic ethnicity as a risk factor (13). The adjusted odds ratio for a lifetime alcohol intake of zero to 18 g/day was greater for Hispanic postmenopausal women compared with non-Hispanic white postmenopausal women (1.36 *vs.* 1.04), as well as for an intake of >19 g/day (1.72 *vs.* 1.22). Results for average lifetime alcohol intake indicated a 24% (95%CI, 0.70-2.19) increase in risk per 13 g/day in Hispanic women compared with 10% (95%CI, 0.99-1.22) in non-Hispanic white women.

Covariates of alcohol intake and breast cancer risk

Most previous studies of alcohol consumption and breast cancer have included several covariates as potential confounders (13, 14, 16, 19, 31, 33, 35, 54, 60, 61). Although the cumulative evidence from studies may suggest a causal link between alcohol and breast cancer, the weak and irregular dose-response association of alcohol and breast cancer is also compatible with confounding by one or more unidentified factors (62). Sorting out which factors are confounders of the association between alcohol and breast cancer is difficult in the absence of any well defined biological mechanism linking alcohol intake to breast tumorigenesis (62). In addition, the link between breast cancer and some important confounders of alcohol intake is not well defined. For example, it is well accepted that higher *vs.* lower socioeconomic status (SES), measured by education or income, is associated with an increased breast cancer risk (63). However, in a study based on the first National Health and Nutrition Examination Survey (NHANES 1), the positive association between higher education and postmenopausal breast cancer risk was attenuated when other factors, including ethnicity, family history of breast cancer, nulliparity, age at first birth, age at menarche, age at menopause, oral contraceptive use,

hormone replacement, alcohol use, BMI, and height were adjusted for. The reproductive risk factors and height had the strongest effect on decreasing the risk from 2.3 (95% CI 1.3-4.2) to 1.5 (95% CI 0.8-2.7) (64).

Family history of breast cancer, reproductive and hormonal factors, diet, physical activity, obesity, and smoking are risk factors that have been evaluated most frequently as confounders or effect modifiers of alcohol consumption and breast cancer. In general, the results of various studies have been inconsistent and, overall, the magnitude of the alcohol-breast cancer association has not been greatly altered by adjustment for these factors (15, 18, 36, 65, 66).

Family history of breast cancer increases risk for breast cancer by 2- to 3-fold, and may interact with other risk factors (67). Atypical hyperplasia, a risk factor for women with breast cancer (OR=3.7), is reported to be almost two-fold higher for women with a family history of breast cancer (OR=7.3) (68). High waist-to-hip ratio (OR=3.2 *vs.* 1.2) and late age at first pregnancy (OR=5.8 *vs.* 2.0) were shown to be stronger risk factors for postmenopausal women (55-69 years) with a family history of breast cancer compared to those without such a history (69). A significant cohort effect for risk of breast cancer was reported for BRCA1 carrier women born post-1930 (RR=2.4) as well as a protective effect for increasing parity (RR=0.9) (70). Bondy et al. reported that Hispanic women with breast cancer were less likely to have a family history of breast cancer than non-Hispanic white or Black women (8). Genetic markers of susceptibility to breast cancer, such as the tumor suppressor genes, BRCA1 (71), BRCA2 (72), and p53 (73) have been discovered that explain a large percentage (about 80%) of familial breast cancer. These genetic markers, however, account for only 5 to 10% of all breast cancers (74). It is likely that a number of other polymorphic genes exist that may be associated with small relative risks, but large attributable risks. It is conceivable that some may affect susceptibility or response to alcohol intake, perhaps by altering metabolic or hormonal pathways.

The expression of estrogen (ER) and progesterone (PR) receptors in breast cancer cells associated with cell differentiation and tumor response to hormonal therapy is partly under genetic control (75). Variability in ER/PR expression could influence susceptibility to the effects of alcohol on the breast or, alternatively, alcohol could be a factor influencing the expression of hormone-receptors in the breast.

In addition to family history, genetic factors, and differences in estrogen receptor expression in the breast, it is also important to consider previous history of benign breast disease as a potential confounder. Fibrocystic disease, also referred to as benign breast disease, is well recognized as a marker of tissue alteration that is associated with an increased risk for subsequent breast cancer (76). It is also well recognized that this is a 'catch-all' term for a variety of proliferative changes that have widely different risks for malignant breast disease (76). It has been suggested that proliferative types are most associated with breast cancer risk, and that atypical hyperplastic lesions are the most important (77, 78). Estimates based on data from the Nurse's Health Study, indicated that women with a history of atypical hyperplasia had almost a four-fold increased risk of breast cancer (OR=3.7 95%CI 2.1-6.8) compared to only a 60 percent increased risk (OR=1.6 95% CI 1.0-2.5) for women with proliferative disease without atypia (68). A higher risk is associated with atypical lobular hyperplasia (OR=5.3 95% CI 2.7-10.4) compared with atypical ductal hyperplasia (OR=2.4, 95% CI 1.3-4.5) (79). It is not known whether past alcohol intake is associated with fibrocystic disease. It is possible that women with a history of fibrocystic disease could be more susceptible to the effects of recent alcohol intake.

A number of reproductive factors have been shown to be associated with an increased risk of breast cancer, such as early age at menarche, late age at FFTB, nulliparity, short duration of lactation, duration of oral contraceptive use, and late menopause (63). It is not clear at this time how these might confound the association of alcohol intake with breast cancer. Theoretically, these reproductive factors are related to breast cancer risk, because they modify endogenous estrogen exposure (46). If the underlying pathogenic mechanism linking alcohol to breast cancer is, in fact, the effect of ethanol intake on circulating estrogen levels (62), then it seems plausible that these reproductive factors could alter either susceptibility or response to alcohol intake. It is important to recognize that some of these reproductive variables, for example age at menarche or age at FFTB, are strongly age-dependent and may define critical periods for alcohol exposure during an individual's lifetime. Relatively little is known about age-specific drinking patterns or how these may interact with critical developmental periods, or with other reproductive variables.

Diet, physical activity, and body fatness are covariates of alcohol intake that may be potential, important confounders of an association between alcohol intake and breast cancer.

Hunter and Willett have extensively reviewed the published literature on associations between diet and breast cancer (80, 81). Many studies have focused on dietary fat intake, but results have been inconclusive. In general, dietary fat is not thought to be a strong risk factor. Howe's meta-analysis of 12 case-control studies found a significant association between daily total fat intake and breast cancer risk (OR=1.35, p = 0.005) (30). Prospective cohort studies, however, do not support the hypothesis that dietary fat intake is associated with breast cancer risk (81). The meta-analyses of Longnecker (15, 33) and Howe (34) suggest that the association between alcohol intake and breast cancer is not due to confounding by total energy or fat intake. Dietary energy and fat intake may be modified by alcohol intake (36). Alcohol is metabolized similarly to fat and can be a significant source of energy (82). Total energy intake and alcohol intake, however, may be only weakly correlated in drinkers with low to moderate intake and even negatively correlated in very heavy drinkers, because alcohol may replace other nutrients, accounting for a greater percentage of total energy (82).

Physical activity has been shown to be associated with a reduced risk of breast cancer in a number of studies (83-85), including ones of Hispanic women (86). For example, Bernstein et al. reported that risk of breast cancer was 60% lower among women who exercised four or more hours per week during their reproductive years compared with inactive women (83). As for many breast cancer risk factors, it has been hypothesized that the effect of physical activity operates by altering estrogen or estrogen-related pathways. A variety of studies have shown that strenuous physical activity affects various reproductive variables, including age at menarche, menstrual cycle length, and total lifetime ovulatory cycles (87). Few studies have looked at confounding or interaction between physical activity and alcohol intake on breast cancer risk. It is plausible that women with higher levels of habitual physical activity are more health conscious and drink less than those with lower levels of physical activity. It is also plausible that regular exercise may alter the metabolism of alcohol or modify its effects on breast tissues.

Increased BMI, a widely accepted measure of body fatness, has been shown to be a risk factor primarily for postmenopausal women, and to have an inverse association to disease risk in premenopausal women (80, 88-90). For example, Trentham-Dietz et al. (90) reported that increases in BMI were associated with a trend towards a protective effect in premenopausal women, but a significant trend towards increased risk in postmenopausal women in a large case-

control study. The odds ratio for highest compared with the lowest quintile of BMI was 0.87 (95%CI 0.70-1.08) in premenopausal women compared with 1.41 (95%CI 1.25-1.60) in postmenopausal women. Increased body fatness is the result of excess energy intake over energy expenditure, and alcohol intake may be associated with increased body fatness if it results in increased energy intake and reduced physical activity. Obesity, or excessive body fatness, is known to be associated with hormonal changes, particularly increased levels of free, or biologically active, estrogens in postmenopausal women in whom adipose tissue acts as a endocrine organ by converting androgens into estrone. Hankinson et al. (91) reported moderate correlations (r-values >0.50) between BMI and plasma estrogens in 217 postmenopausal women without breast cancer from the Nurses' Health Study. A weak, but statistically significant correlation ($r = 0.17$, $p < 0.05$) was found between recent alcohol intake, based on a food frequency questionnaire, and plasma estrone-sulfate after adjusting for age and BMI. Correlations of alcohol with total and free-estradiol and estrone were much weaker and not significant. These data support the hypothesis that recent alcohol intake and current level of obesity, at least, are independently associated with circulating estrogen levels and, therefore, could have independent effects on breast cancer risk.

Although smoking has historically been considered unimportant in the etiology of breast cancer (92), recent evidence suggests the contrary (93). Some studies have reported increased breast cancer risk for heavy smokers who began smoking at an early age or who smoked for many years (94). Smoking has also been hypothesized to have anti-estrogenic effects, in addition to carcinogenic effects, which could obscure the overall effect on breast or other hormone-dependent cancers (95). In a recent study, Gammon et al. (94) reported that current smoking had an inverse association with breast cancer in premenopausal women, particularly in those who started smoking at an early age (OR=0.59, 95%CI 0.41-0.85) or who had smoked for >21 years (OR=0.70, 95%CI 0.52-0.94). Some data indicate that smokers tend to consume more alcohol than non-smokers (96). It is therefore relevant that in the Gammon study, the odds ratio for current smoking was 0.68 (95%CI 0.47-0.98) in non-drinkers, but increased to 1.21 (95%CI 0.67-2.19) in those drinking >7 drinks/week (94).

Stratification on menopausal status has been shown to be important with regard to the effects of several risk factors on breast cancer risk (97), including alcohol. In Longnecker's case-

control study (16), alcohol intake >13 g/day before 30 years of age was associated with an increased risk (OR = 1.34, 95%CI 1.02-1.75) in premenopausal women, but recent consumption >13 g/day was not (OR = 1.05, 95%CI 0.85-1.31). This pattern was reversed in postmenopausal women in whom risk was increased for recent intake (OR=1.26, 95% CI 1.12-1.42), but not for intake prior to 30 years of age (OR=1.02, 95%CI 0.88-1.20).

Summary

In summary, a majority of both case-control and cohort studies indicate an increased prevalence of alcohol intake in cases, an increased incidence of breast cancer in those drinking ≥14 g/day of alcohol, an increased risk associated with dose, as well as risk differential associated with timing of exposure (recent *vs.* past alcohol intake). In general, these risks do not seem to differ by beverage type, suggesting that ethanol is the actual risk factor. Although there are few studies of hormone-receptor breast tumor subtypes, the results suggest that receptor status outcome may vary due to different risk factors.

The weight of experimental animal studies does not tend to support the alcohol-breast cancer risk hypothesis. However, small human clinical studies have suggested that alcohol may exert an effect on breast cancer risk by increasing estrogen levels. These changes might increase susceptibility to breast cancer carcinogens by acting as promoters. Although the scanty results from animal experiments have been inconsistent for breast tumorigenesis, alcohol is still an established carcinogen for other cancer sites and its effect on serum hormone levels has been identified (18).

By analogy, the pattern for the association between breast cancer and alcohol, as well as other known or considered risk factors, does not appear dissimilar. Certainly, the risk associated with several of the reproductive factors (early age at menarche, late age at menopause, absence or short duration of breastfeeding) is within the 1.5 to 2.0 range (98), which covers the estimate generally reported for alcohol and breast cancer. Although not all studies investigating the alcohol-breast cancer association were conducted with an '*a priori*' hypothesis, and the effect is modest, there is a consistency in the trend and magnitude of the well-designed large studies (99).

BODY

MATERIALS and METHODS

The data for this study were drawn from the 'New Mexico Women's Health Study' (NMWHS), a statewide population-based case-control study of breast cancer in Hispanic and non-Hispanic white women. Incident cases diagnosed with an invasive or *in situ* breast carcinoma during the period January 1, 1992 through December 31, 1994, who were aged 30 through 74 years of age and residents of New Mexico at diagnosis, were eligible for the study. Cases were ascertained through the New Mexico Tumor Registry's (NMTR) rapid ascertainment system.

Selection of case subjects

All eligible Hispanic cases were included. Hispanic ethnicity was based on Spanish surname identified by means of a computer program based on the 1980 Census Bureau list of Spanish surnames, and a computer program (GUESS) that evaluates beginnings, endings and specific letter combinations in a last name (100). The overall expected number of breast cancer cases for the study period was approximately three times higher for non-Hispanic cases compared with Hispanics. A random sample of approximately 33% of non-Hispanic white cases based on age group (30-39, 40-64, 65-74 years) and geographic region, defined by seven state health planning districts, was identified for inclusion. The sampling fraction for non-Hispanic whites in each of these 21 strata was chosen to give a distribution similar to the age and geographic distribution of Hispanic cases ascertained by the NMTR in the three-year period 1988 through 1990. There was a total of 491 eligible Hispanic breast cancer cases. Random selection of non-Hispanic whites resulted in 493 cases. Of the eligible cases, 332 Hispanic (68%) and 380 non-Hispanic white women (77%) completed interviews.

Selection of control subjects

Controls were frequency-matched on the basis of Hispanic and non-Hispanic white ethnicity, three age groups (30-39, 40-64, 65-74), and seven health planning districts. Controls were ascertained through a modified approach to the Waksberg random digit dialing method (101). Data from the NMTR collected over the past 26 years were used to build a pool of prefixes known to contain residential numbers for control selection. This pool was based on those prefixes which had contributed at least one breast cancer case to the NMTR database. This

restricted pool of prefixes was used to increase the likelihood of generating a larger pool of 'working' residential phone numbers; a real concern due to the sparsely populated counties of New Mexico. Additionally, a random sample of phone numbers linked to gender, health planning district, ethnicity, and age-group were used to efficiently locate and recruit a sufficient number of older, rural Hispanic controls due to the difficulty in ascertaining this subset of women.

A total of 8,147 working telephone numbers were contacted; of these, 4,459 were residential numbers. There were a total of 1,039 eligible controls ascertained from 3,400 respondents who completed the telephone screening interview; 511 Hispanic and 528 non-Hispanic white women. Of these, 388 (76%) Hispanic, and 456 (86%) non-Hispanic white women completed interviews. Overall response rates for controls, stratified by ethnicity, could not be calculated because ethnicity of non-respondents was unknown.

Data collection

The University of New Mexico's Human Research and Review Committee approved the NMWHS project. Physician consent was obtained for all cases and a written informed consent was signed at the onset of the interview. Interviews were conducted in-person at a subject's home or an agreed upon location and averaged 1½ hours. All questionnaires were translated into Spanish, and interviews were conducted in Spanish or English by bilingual interviewers according to the participant's preference.

Recent dietary and alcohol intake was collected at the beginning of the interview, using a modified version of a quantitative food frequency questionnaire (FFQ) designed by the staff of the Human Nutrition Center at the University of Texas-Houston, School of Public Health. This FFQ was previously used in a Texas Hispanic population (102). Modifications, based on an analysis of food intake recalls of 100 women, were made by Dr. RS McPherson to add foods to the FFQ that were important sources of nutrients among New Mexico women. The final FFQ instrument was developed using standard protocols and included 140 items (103, 104). Frequency of use information included consumption on a per month (28 day), week, or day basis and portion size consumed. Two-dimensional food models were used to aid in the determination of amount consumed. Frequency of consumption and portion size data were entered into the 'Food Frequency Data Entry and Analysis Program' containing the gram weight and nutrient data

to calculate nutrient estimates per food per day, and total nutrient intake per day (105, 106). In an effort to avoid the potential impact of disease or treatment on diet, all subjects were asked to recall 'usual' food intake for a four-week period, six months prior to the interview.

'Recent' alcohol intake, as measured by the FFQ, was expressed as the average daily consumption of the summation of wine, beer, and hard-liquor intake. This was converted to a weekly intake for analysis. The ethanol content for each type of beverage was based on the amount reported in the US Department of Agriculture (USDA) Nutrient Database for Individual Intake Surveys: 8.132 g/alcohol for one 3 ½-ounce glass of wine; 12.6 g/alcohol for one serving of beer; and 21.2 g/alcohol for one hard-liquor drink (106). Alcohol abstinence (nondrinkers) was defined as an intake of 0 g/day.

A 'Risk Factor Questionnaire' (RFQ) was used to collect data on demographic characteristics and breast cancer risk factors. A calendar was used to record major life events as an assistance to recall. Data on breast cancer risk factors were collected for a variety of factors, including reproductive and menstrual history, use of oral contraceptives and exogenous hormones, family history and personal history of breast disease, weight, height, physical activity during the prior year, history of cigarette smoking, and alcohol consumption. The questions on alcohol intake included ever *vs.* never use, age at first use, age at cessation, frequency of drinking, and number of weekly drinks by beverage type at age 25, 35 and 50 years. Frequency of drinking included daily, weekly, monthly and yearly categories. The number of drinks per week for subjects reporting consumption on a monthly or yearly basis was estimated based on the frequency midpoint divided by the number of weeks per time interval. The ethanol content in grams was multiplied by the number of weekly drinks per beverage type to estimate gram intake/week.

Hormone-receptor assays were conducted in laboratories associated with the hospitals where cases were diagnosed. Estrogen and progesterone receptor status are separately coded by the SEER Program as: none done (0); positive (1); negative (2); borderline or undetermined (3); ordered, but results not in chart (8); and unknown (9). Breast cancers were categorized by the joint classification of ER/PR status (ER+PR+, ER+PR-, ER-PR+, ER-PR-, unknown). If either ER or PR status was unknown, the joint status was considered 'unknown'.

The criteria used to classify menopausal status have been described elsewhere in a previous analysis of reproductive factors (107). Final categories included premenopausal, postmenopausal, and surgical unknown, based on self-report of menstrual history, history of hysterectomy with or without oophorectomy, and use of estrogen replacement therapy. Menopausal status was classified at the date of interview for controls and the date of cancer diagnosis for cases. Women were classified as premenopausal if they reported a menstrual period within one year of the reference date, and were not taking estrogen at the time of their last period. Women were classified as naturally postmenopausal if they had not had a period for at least one year prior to the reference date or were taking estrogens at the time of their last period, and had not had a bilateral oophorectomy in either case. If a woman reported having a bilateral oophorectomy within one year of her last period then she was classified as surgically postmenopausal. Women who reported a first use of estrogens within one year of a hysterectomy with or without a report of a bilateral oophorectomy were classified as having post surgical menopause. Finally, women who reported having a hysterectomy without bilateral oophorectomy within one year of their last period, and were not placed on estrogens within one year of the surgery were considered to have an unknown menopausal status. For women with unknown status, the ethnic-specific distribution of age at menopause among controls was used to assign menopausal status. Premenopausal status was assigned to women with unknown status whose ages fell below the 10^{th} percentile (43 years) of this distribution, and postmenopausal status to women whose ages fell above the 90^{th} percentile (54 years). Age at menopause was defined as the age at last natural menstrual cycle followed by one year of amenorrhea, after one year of hormone replacement therapy, or at the date of bilateral oophorectomy.

Body mass index (BMI) was calculated as weight in kilograms(kg)/height in meters squared(m^2). Metabolic equivalents (METS) were calculated for physical activity as kilocalories (kcals)/kg of weight/hour (108). The assigned metabolic equivalents were multiplied by the mean number of hours/week to compute final METS.

STATISTICAL METHODS

Conditional multivariate logistic regression was used to determine age-adjusted and multivariate odds ratios and corresponding 95 percent confidence intervals for alcohol exposure variables adjusting for covariates (109). Logistic regression analyses based on all subjects were

conditioned on the three matching factors (three age-groups, seven health planning districts, Hispanic and non-Hispanic white ethnicity). Ethnic-specific logistic regression analyses were conditioned on the matching factors age-group and health planning district. Polytomous logistic regression analysis was used to estimate odds ratios for the joint classification of hormone-receptor status, when both receptors were known, relative to controls. Joint categories included (ER+PR+, ER-PR-, ER+PR-, ER-PR+) (109). Logistic regression analyses were computed using STATA software (110).

The alcohol exposure variables investigated included recent intake collected on the FFQ, and history of alcohol consumption defined as ever *vs.* never use, status of alcohol consumption at time of interview (nondrinker, current drinker, former drinker), age at first use, years since last consumption, years of drinking, gram intake/week at ages 25, 35, and 50, and average lifetime intake based on data for the latter three ages, as collected on the RFQ. Specific beverage type was not analyzed, because there has not been consistent evidence to suggest an effect independent of ethanol content (15, 17, 18, 60). Additionally, it is difficult to estimate the separate effects due to each beverage type, since women tend to drink a combination of alcoholic beverages (14).

The covariates considered in the present analyses were selected based on previous studies. These are discussed in the previous section, 'Covariates of Alcohol Intake and Breast Cancer Risk' (page 20). These included: education; age at menarche; age at first full-term birth (FFTB) for pregnancies lasting six months or longer regardless of pregnancy outcome; number of full-term births lasting six months or longer (single birth, multiple birth, stillbirth); cumulative months of lactation for all children; cumulative years of oral contraceptive use; menopausal status, history of fibrocystic disease; breast cancer in mother, sister, or daughter; history of cigarette smoking lasting for more than six months; usual adult BMI (based on reported 'usual' adult weight and reported height at interview; physical activity; energy intake; and energy-adjusted total fat intake. Analyses were also stratified by ethnicity and menopausal status to evaluate whether different sets of confounders were important across strata. The logistic regression models included all covariates to allow comparison of results between ethnic and menopausal status groups. The change-in-estimate method was used to identify the most important confounders within each ethnic and menopausal specific model by comparing models

containing all covariates with models excluding each covariate (111). Interaction between menopausal status and alcohol was investigated by comparing models, with and without product terms, using the log likelihood test statistic (109). Menopausal status may be a marker for change in endogenous hormones, and therefore a critical effect-modifier of the alcohol-breast cancer association (13). It was included in all models, because it has been shown to be important in previous analyses of reproductive variables for the NMWHS (107).

Age, defined as age at diagnosis for cases and age at interview for controls, was included in all models to adjust for residual age differences between cases and controls. Category boundaries for covariates that were not dichotomous were defined either on the basis of commonly accepted cutpoints, or on the basis of the distribution among controls. Alcohol-related variables were categorized by the number of grams/week. Categorical variables were evaluated to determine whether final groupings were too few to detect dose-response changes or too many to provide stable estimates (111). Total fat intake was highly correlated with energy intake (Spearman's rank correlation coefficient, r=0.91), and was energy-adjusted based on the residual method (112). Alcohol use was not energy-adjusted as it was weakly correlated with total energy intake (r=0.15), as shown in other studies (112).

Several factors reduced sample sizes for some analyses. There were five non-Hispanic white controls in age group 30-39, planning districts 4 and 5, and four Hispanic controls in age group 30-39, planning district 5, and age group 65-74, planning district 1, who were dropped from the conditional logistic regression analyses because there were no cases in those particular strata. As a result, the total sample size for the logistic regression analyses was based on 1,547 subjects (716 Hispanic, 831 non-Hispanic white).

Subjects with an energy intake outside the range of 500-6,000 kcals were excluded. Exclusions were due to 16 subjects with an energy intake >6,000 kcals/day, and all but one had a low alcohol intake <10 g/day. An evaluation of the 'past' alcohol exposure variables included the recoding for 30 subjects from drinkers to non-drinkers, because their first age and stop age for alcohol consumption was the same. These subjects reported no past use of alcohol for any of the age points; 73% of this group reported a first age of 25 years or less, and only four reported an age at first use to be 35 or greater. Seven subjects were excluded due to incomplete or no

FFQ data. Additional deletions were related to missing data for covariates included in the models.

Relevant covariates were evaluated in combined and ethnic-specific analyses. Most previous studies have categorized these variables. Category boundaries for variables that were not dichotomous were defined either on the basis of commonly accepted cutpoints, or on the basis of the quantile distributions among combined controls. Categorized variables were evaluated to determine whether final groupings were too broad to detect dose-response changes or too narrow to provide stable estimates (111). All data analyses were performed using SAS (113) and STATA (110). Conditional logistic regression analyses were made using STATA procedures (110).

RESULTS

Descriptive statistics

The majority of cases were diagnosed with intraductal carcinoma (66%), followed by lobular carcinoma (9%), comedocarcinoma (6%), and infiltrating ductal and lobular carcinoma (5%). Although frequency of stage at diagnosis followed the same trend for both ethnic groups, regional disease at diagnosis was somewhat higher for Hispanic women (33%) compared with non-Hispanic white women (24%). Local disease and *in situ* stage was likewise lower for Hispanic women (49% and 14%) compared with non-Hispanic white women (54% and 19%).

The mean age of cases at diagnosis was 54 years (Standard deviation, [SD]=11) compared with 52 years (SD=12) for controls at time of interview. Only a small percentage of interviews were conducted in Spanish (3%), and 93% were home-interviews. The majority of Hispanic subjects were lifelong New Mexico residents (75%), compared with non-Hispanic whites (15%). Table 1 describes the distributions of demographic variables by ethnicity and case-control status. Distribution of selected characteristics for cases and controls have been previously reported (107). Hispanic women, compared with non-Hispanic white women, were generally younger at their FFTB, had a higher parity, greater BMI (>=23 kg/m^2), and less education (107). They did not report a history of fibrocystic disease or a family history of breast cancer as frequently as non-Hispanic whites (107). Hispanics (35 percent) reported no physical activity or a non-vigorous level more frequently than non-Hispanic whites (23 percent). In general, Hispanic

women, compared with non-Hispanic white women, reported slightly higher median levels of daily total energy intake (2,257 *vs.* 2,108 kcals/day) and total fat intake (85 *vs.* 80 g/day).

Hispanic women reported a history of 'ever' alcohol consumption less frequently than non-Hispanic white women (77 *vs.* 88 percent), and cases were similar to controls (81 *vs.* 85 percent). Overall, 42 percent of cases and 48 percent of controls reported recent alcohol intake during the one month period, six months prior to interview. Table 2 shows distributions for alcohol exposure variables by ethnicity and case-control status. Status of drinking at interview showed that cases reported being 'current' drinkers about 10% less frequently than controls, with controls reporting an earlier age at first use. Hispanic women reported alcohol intake at ages 25, 35, and 50 less frequently compared to non-Hispanic white women (Table 3). Consumption of alcohol on a daily or weekly level was very low at all three ages, especially in Hispanic women who reported daily and weekly intakes about one-half as often as non-Hispanic whites (Table 4). Intake for these three age periods was combined when appropriate for an approximate lifetime average (Table 4). Few women reported drinking more than four drinks per week as a lifetime average.

Alcohol intake based on the FFQ daily gram estimate showed that only 47% of all subjects reported alcohol consumption in the four-week period six months prior to the interview. Reported recent alcohol intake was low with 55 percent of Hispanics and 38 percent of non-Hispanic whites reporting an intake of less than one drink/week, and only a small percentage reporting more than four drinks/week (Table 4). Similar to past alcohol intake estimates, the overall level of consumption reported on the FFQ was higher in non-Hispanic white compared to Hispanic women.

Co-morbid conditions were similar in distribution by both case-control status and ethnicity with the exception of diabetes, gallbladder disease, and rheumatoid arthritis, which were higher in Hispanic women, at 12%, 19%, and 11%, compared with non-Hispanic white women at 4%, 13%, and 6%, respectively.

Age-adjusted covariates

Age-adjusted odds ratios for breast cancer risk factors are shown in Table 5. Patterns differed by ethnicity. A high BMI was the strongest statistically significant risk factor (OR=2.38

for >=25.6 kg/m^2) and vigorous physical activity was the strongest protective factor (OR=0.34 for >=35 METS)/week) among Hispanic women. Among non-Hispanic whites, a positive history of fibrocystic disease (OR=1.68) was the strongest risk factor, whereas 12 months or more of lactation (OR=0.53), and vigorous physical activity (OR=0.55 for >=35 METS/week) were strong protective factors. High intake of energy and total fat appeared to be protective in non-Hispanic whites, but not in Hispanics. All covariates listed in Table 5 were kept in the final models, so comparisons could be made across ethnic and menopausal status groups. The effects of specific covariates are described below. Results for menopausal status did not show the same trend in both ethnic groups.

Although both variables, education and income, were evaluated at the univariate level, education was selected for further evaluation as a confounder because the two variables were correlated (Spearman's rank correlation coefficient, r=0.46), and income compared with education was missing for more subjects (59 *vs.* 6). The measures of body mass index, 'usual' and past index at 18 years of age also were highly correlated (r=0.51). 'Usual' BMI was selected to include in analyses because it is more likely to be associated with both recent and past alcohol intake than BMI at age 18.

Recent alcohol intake

Data from a previous pilot study were used to assess the validity and reproducibility of alcohol intake as measured by the FFQ. These data were based on 132 volunteer New Mexico Hispanic and non-Hispanic white women, aged 35 to 74 years, with and without a breast cancer history (114). The Spearman correlation coefficient between alcohol intake during the past month and intake for the same month, recalled six months later, was 0.83. Results were comparable for cases (r=0.82) and noncases (r=0.85), but were lower for Hispanics (r=0.73) compared with non-Hispanic whites (r=0.87). This reproducibility for alcohol intake is comparable to that reported in previous studies (61, 115, 116).

The age-adjusted odds ratio for recent alcohol intake was 1.42 (95 percent CI 0.82-2.46) for non-Hispanic white women consuming >=148 g/week (8+ drinks/week), and 1.14 (95 percent CI 0.56-2.29) for Hispanic women consuming >=85 g/week (5+ drinks/week) as compared to nondrinkers (Table 6). Multivariate adjustment increased these odds ratios to 1.56 (95 percent CI 0.85-2.86) and 1.35 (95 percent CI 0.63-2.93), respectively (Table 6). Low level of recent

alcohol intake (<8 drinks/week) was associated with a consistent reduced risk of approximately 50 percent in the multivariate full model for non-Hispanic white women (Table 6). Overall, there was no evidence of an alcohol effect on breast cancer risk in Hispanic women.

Analyses based on reduced models including the strongest ethnic-menopausal confounders (>=20 percent change in the odds ratio, Table 7), did not produce estimates that were substantially different from the full models containing all covariates or the age-adjusted models. In a reduced model for Hispanic women (Table 8), in which fibrocystic disease and smoking were excluded, point estimates differed from those in the corresponding full model (Table 6) by 11 percent or less, with the greatest difference present for the highest alcohol intake (8-<148 g/week or5-7 drinks/week). In non-Hispanic white women, a reduced model including only age, energy intake, and cigarette smoking, and BMI, produced an odds ratio of 1.65 (95 percent CI 0.93-2.92) for the highest level of alcohol intake (>=148 g/week), and odds ratios ranging from 0.49 to 0.72 for alcohol intake levels less than 148 g/week (Table 8). Further elimination of cigarette smoking from the reduced model for non-Hispanic whites produced the same results for all intake levels, with the exception of the highest level which was reduced to the same estimate as shown for the full model (OR=1.56) (data not shown). Table 9 shows results for the same analyses stratified by menopausal status. On average, across ethnic and menopausal groups, the estimates based on the reduced models did not differ by more than 15 percent from the full models, and did not always enhance the magnitude of the effects. In general, no strong confounders of alcohol intake and breast cancer emerged in the analyses. The comparison of full *vs.* reduced *vs.* age-adjusted models did not suggest any problems with overfitting due to the inclusion of all covariates in the full models (109).

Recent alcohol intake was further collapsed into fewer categories, based on lack of trend. These included four categories (nondrinker, <8, 8-<42, >=42 grams/week) for Hispanics, and three categories (nondrinker, <148, >=148 grams/week) for non-Hispanic whites. Among non-Hispanic white women, there was a statistically significant reduced risk for breast cancer (OR=0.49, 95 percent CI 0.35-0.69) among women reporting fewer than 8 drinks/week compared to nondrinkers. This reduced risk for low alcohol intake was also present for premenopausal (OR=0.29, 95 percent CI 0.15-0.56) and postmenopausal non-Hispanic white women (OR=0.56, 95 percent CI 0.35-0.90) (Table 10). There was no consistent evidence for a protective effect of low

to moderate alcohol intake in Hispanics by menopausal status. There was a suggestion of an increased risk at the highest level among postmenopausal women for both ethnic groups, but estimates were unstable and statistically nonsignificant (Table 10).

Hormone-receptor status and recent alcohol intake

The distribution for ethnic-specific hormone-receptor status was similar with the exception of ER-/PR- (24 percent for Hispanic *vs.* 17 percent for non-Hispanic white) (Table 11). About 40 percent in each ethnic group were ER+/PR+; 10 to 12 percent were ER+/PR-; 3 percent were ER-/PR+; and 9 to 12 percent were unknown. In the polytomous logistic regression analysis of recent alcohol intake, only ER+/PR+ and ER-/PR- were included, and each case group compared simultaneously with the controls. Stratification was limited to ethnicity as stratum-specific numbers were too small to additionally stratify by menopausal status. The direction of the odds ratios was similar for the two hormone-receptor status groups (Table 12). Among non-Hispanic white women, odds ratios for ER+/PR+ status were statistically significant for both low (OR=0.46, 95 percent CI 0.28-0.74), and high alcohol intake (OR=2.13, 95 percent CI 1.03-4.43) (Table 12). An increased risk for non-Hispanic whites associated with an intake of 8+ drinks/week was 50 percent higher for ER+PR+ compared with ER-PR- status, but the difference was not statistically significant. There was no clear trend or significant results by hormone receptor status for Hispanic women.

Past alcohol intake

Age-adjusted odds ratios for alcohol exposure variables are shown in Table 6. Alcohol consumption (ever *vs.* never), showed a modest protective effect, although not statistically significant (OR=0.80, 95%CI 0.60-1.06). This protective effect was significant, however, for all women who were current drinkers (OR=0.70, 95%CI 0.52-0.94), in contrast with former drinkers who showed a slightly increased risk. The association in former drinkers was further found to be due primarily to cases (n=44) who reported that they stopped drinking at the time of diagnosis (overall OR=8.98, 95%CI 3.41-23.66). Risk was also increased, although to a much lesser extent, in those who stopped drinking within one to four years prior to diagnosis in both ethnic groups. In general, women who stopped drinking five or more years prior to diagnosis showed a decreased risk. Current drinkers also showed a significant protective effect for all women combined (overall OR=0.72, 95%CI 0.54-0.97).

Results for ever *vs.* never alcohol consumption did not show a significant association with breast cancer in the age-adjusted analysis for Hispanic women (OR=0.78, 95 percent CI 0.54-1.14), or for non-Hispanic white women (OR=0.76, 95 percent CI 0.49-1.19) (Table 13). Multivariate adjustment did not alter these results (Table 13). Multivariate analyses were performed to test for interaction between menopausal status and ever *vs.* never alcohol intake. Inclusion of an interaction term increased the main effect estimate for 'ever' alcohol intake to increase by 50 percent, but results were not statistically significant for either ethnic group (Hispanic: -2 log likelihood test statistic: χ^2= 1.56, p=0.21; non-Hispanic white: χ^2= 0.04, p=0.84).

Risk of breast cancer did not vary by age at first use or by duration of drinking (Table 13). There was no suggestion of an alcohol effect for lifetime average intake or for ages 25, 35, and 50 (Table 14). Overall, most risk estimates were less than 1.0, and none were statistically significant. A minimal risk for Hispanic and non-Hispanic white former drinkers was present, but this was due primarily to the 44 cases who reported cessation of drinking within year of diagnosis (OR=12.13 for Hispanic; OR=8.04 for non-Hispanic white, Table 13). Risk decreased as years since last alcohol consumption increased (Table 13). These cases had more severe disease (regional/remote) at diagnosis (58 *vs.* 42 percent), were younger (48 *vs.* 54 years) than other cases, and reported the lowest level of average lifetime alcohol intake (32 *vs.* 48 g/week). Table 15 provides a comparison of selected characteristics for these women compared to other cases. Exclusion of this group produced estimates close to 1.0 for former drinkers among Hispanics (OR=0.94, 95 percent CI 0.53-1.56) and non-Hispanic whites (OR=0.86, 95 percent CI 0.648-1.55) (Table 16). All other analyses of past and recent alcohol intake were no more than 10 percent different when these subjects were excluded (Table 16).

KEY RESEARCH ACCOMPLISHMENTS

- Further training in epidemiologic methods, cancer epidemiology with an emphasis on breast cancer, and biostatistical methods.
- Completion of the doctoral dissertation and doctoral (PhD) degree through the University of Texas-Health Science Center, The School of Public Health, Houston, Texas.
- Advancement of research and employment opportunities as a direct result of training from this predoctoral fellowship training grant (see details below).
- Application for funding as a Co-investigator on several studies directly related to breast cancer research, with plans to take on the Principal Investigator role on two of them (#1 and #2 - see study titles below).

REPORTABLE OUTCOMES

In compliance with the original 'Statement of Work' (see Appendix II), the following section reviews the reportable outcomes for each of the three grant years.

YEAR 01 - COMPLETED TASKS

During the first performance period (September 1, 1996 - August 31, 1997) of the predoctoral fellowship, an advisory committee was formed in the Fall, 1996 at The University of Texas School of Public Health, Houston, Texas (UTSPH), and was composed of: Dr. John F. Annegers, Professor of Epidemiology; Dr. Ralph Frankowski, Professor of Biometry; and Dr. R. Sue McPherson, Associate Professor of Epidemiology and Nutrition. The required number of courses was completed prior to taking the doctoral qualifying exam under the supervision of the advisory committee. The principal investigator attended the 30th Annual Meeting for the Society for Epidemiologic Research, held from June 12 - 14, 1997 in Edmonton, Alberta, Canada. The qualifying examination was completed satisfactorily in August, 1997, permitting admission to candidacy for a doctoral degree (see Appendix III).

YEAR 02 - COMPLETED TASKS

During the second performance period (September 1, 1997 - August 31, 1998) library research was conducted towards the Ph.D. proposal, the dissertation, and data analysis was initiated. Dissertation research courses in compliance with the UTSPH guidelines were taken, and additional courses were taken in 'Epidemiologic Design and Analysis', 'Causal Inference',

and a one-day workshop on 'Molecular Epidemiology' (see below). A complete list of courses taken is provided in Appendix III. A request to appoint a Ph.D. doctoral thesis committee was submitted in the Fall, 1997 and was approved. A revision was made to include Dr. Jonathan M. Samet, Professor and Chairman of Epidemiology at Johns Hopkins University, School of Hygiene and Public Health, who was the original Principal Investigator of the 'New Mexico Women's Health Study'. This revision was approved in April, 1998 (see Appendix III). Approval was granted by the Associate Dean for Research at UTSPH in January, 1998 to begin work on the doctoral dissertation (see Appendix III). The principal investigator attended the 31th Annual Meeting for the Society for Epidemiologic Research, held from June 24 - 26, 1998 in Chicago, Illinois, and participated in the one-day sponsored "American College of Epidemiology/Society for Epidemiology Research" Workshop on "Genetic Fundamentals for Molecular Epidemiology" held June 23, 1998.

YEAR 03 - COMPLETED TASKS

The scope of work was completed during the third and final performance period (September 1, 1998 - August 31, 1999), with the completion of the doctoral dissertation (see Appendix I). The doctoral dissertation was completed to meet the standards for an article submitted for publication to a peer-reviewed journal. The formal presentation of the doctoral work and dissertation was presented at UTSPH on May 5, 1999 (see Appendix IV). A copy of the doctoral diploma is provided in Appendix III. The core of the dissertation provided in Appendix I is being submitted for consideration for publication.

The completion of the training grant and subsequent doctoral degree has allowed the principal investigator to return to work at the University of New Mexico, Health Science Center, Epidemiology and Cancer Control Program and New Mexico Tumor Registry as an Epidemiologist. The process for a faculty appointment at the level of Research Assistant Professor is in progress. The Principal Investigator has recently been involved in submitting several grants that have received notification of award. These include the following studies: 1) 'The 4-Corners Breast and Endometrial Cancer' study (1R01 CA78762-01A1), National Institutes of Health; 2) 'Assessing Quality of Life Among Breast Cancer Survivors' through the National Cancer Institute's, Surveillance, Epidemiology and End Results Program (SEER No. N01-PC-67007); and 3) 'The Interaction of Genetic Susceptibility and Hormonal Exposures in Breast

Cancer Prognosis' as an additional component to an on-going breast cancer prognosis study ('Weight, Physical Activity, Diet and Breast Cancer Prognosis New Mexico Women's Health Study'), also through the National Cancer Institute's, Surveillance, Epidemiology and End Results Program (SEER No. N01-PC-67007).

Finally, the Principal Investigator will attend the U.S. Army Medical Research and Materiel Command, Breast Cancer Research Program, Era of Hope Meeting to be held June 8-12, 2000 in Atlanta, Georgia to present the results of this research. The preliminary title of the presentation has been submitted as, "Alcohol Consumption and Breast Cancer Risk Among Hispanic and non-Hispanic White Women in New Mexico". The following provides a summary of findings in the submitted abstract (September 14, 1999).

- Alcohol consumption and risk of breast cancer was investigated using the data collected for a New Mexico statewide population-based case-control study. The New Mexico Tumor Registry ascertained women, newly diagnosed with breast cancer (1992-1994) aged 30-74 years. Controls were identified by random digit dialing and were frequency-matched for ethnicity, age-group, and health planning district. In-person interviews of 712 cases and 844 controls were conducted.
- Recent alcohol intake data was collected for a four-week period, six months prior to interview. Past alcohol intake included information on alcohol consumption at ages 25, 35, and 50. History of alcohol consumption was reported by 81% of cases and 85% of controls. Overall, 42% of cases and 48% of controls reported recent alcohol intake.
- Results for past alcohol intake did not show any trend with breast cancer risk, and were statistically nonsignificant.
- Multivariate-adjusted odds ratios for recent alcohol intake and breast cancer suggested an increased risk at the highest level for both ethnic groups, but estimates were unstable and statistically nonsignificant.
- Low level of recent alcohol intake (<148 grams/week) was associated with a reduced risk for non-Hispanic white women (Odds Ratio (OR)=0.5 95% Confidence Interval (CI) 0.35-0.69). This pattern was independent of hormone-receptor status. The reduced breast cancer risk for low alcohol intake was present for premenopausal (OR=0.3, 95% CI 0.2-0.6) and postmenopausal non-Hispanic white women (OR=0.6, 95% CI 0.4-0.9).
- The possibility of an increased risk associated with high alcohol intake could not be adequately addressed, because there were few drinkers with more than light to moderate intake, especially among Hispanic women.
- It is unlikely that alcohol intake explains the increasing incidence of breast cancer in New Mexico Hispanic women, because there appears to be no consistent relationship in the low to moderate range observed, and high alcohol intake is rare.

CONCLUSIONS

A consistent finding in this study was a protective effect for light to moderate alcohol intake (<8 drinks/week) in non-Hispanic white women. However, results were only statistically significant for recent intake. There was a suggestion of an increased risk for breast cancer among postmenopausal Hispanic and non-Hispanic white women at the highest alcohol intake level, and that menopausal status may be an effect-modifier in Hispanic women. The latter finding has been suggested in previous studies (16, 31, 34, 117, 118), but results have not always been consistent. Results for age at first use of alcohol and duration of drinking did not show a risk for breast cancer, but these have not been consistent risk factors (35, 119-121). The pattern of a protective effect at low alcohol intake, and a suggested risk at higher intake in non-Hispanic white women was seen regardless of hormone-receptor status. Investigations of hormone-receptor status and breast cancer risk factors have not shown a consistent association for other risk factors (reproductive-related, smoking, BMI, diet) (19, 24, 25, 53, 122, 123). It is difficult to determine whether differences between hormone-receptor cancer type is associated with etiologic factors or to biological changes that occur during breast cancer development (26).

Generally, studies have demonstrated a consistent, but modest, increased risk with high alcohol intake, differing as to whether the effect is stronger for recent (14, 60, 61) or lifetime intake (13, 16). Results based on a recent analysis of the Framingham cohort did not show any evidence for an increased risk of breast cancer associated with long-term, light to moderate alcohol consumption (66). The majority of studies have found evidence for a dose-response relationship (18), also supported in several meta-analyses (15, 33, 60). Longnecker et al.'s case-control study results (16), based on 15,825 subjects, showed a monotonic dose-response relationship for all women, but strongest for postmenopausal women. Swanson et al. (14) reported a threshold for increased risk at high levels of intake (≥14 drinks/week) for premenopausal women. The data from the present study suggest a weak association for a risk threshold, but at a lower level of intake than previously reported (14), and among only postmenopausal women. The suggestion of a greater alcohol-breast cancer association among postmenopausal Hispanic women, compared with non-Hispanic white women, as reported in Longnecker et al.'s study (13), was not replicated. Hispanic postmenopausal women were

similar to non-Hispanic white women with about a two-fold increased risk, but at fewer drinks/week (3+ *vs.* 8+); however, these estimates were unstable and not statistically significant.

The present study was not able to evaluate heavy alcohol consumption, especially among Hispanics, because there were so few drinkers with a high intake. The relatively low level of alcohol consumption observed in this study has been reported previously in another New Mexico study (58). Studies in other regions of the US have also reported a lower average alcohol intake for Hispanics compared with non-Hispanics (3 *vs.* 5 drinks/week) (11, 124).

A lower response rate was observed in the present study for Hispanics compared with non-Hispanic whites. Response rates for cases were lower than for controls, and lower than that reported by Swanson et al. (86 percent) (14), but fell into the range reported by Longnecker et al. across several states in a multi-centered study (74-86 percent) (16). Response rates for controls were comparable to that for previous studies (14, 16).

It is not possible to determine at this time whether the protective effect observed in non-Hispanic white women for low to moderate alcohol intake is indirect and due to confounding with other unadjusted health-related behaviors, due to an undetected information bias, or due to a direct biological effect inhibiting breast cancer induction or promotion. There was no single strong confounder of alcohol intake that explained the pattern in either ethnic group. This suggests that both the protective effect, as well as the possible threshold for increased risk, observed in non-Hispanic white women, is not due to the confounders included in analysis. Information bias could explain the reduced risk in non-Hispanic white cases if they systematically underreported their true alcohol intake. Previous studies of the effect of recall bias on reported alcohol consumption, however, have found little evidence for more than a modest effect when comparing retrospective to prospective assessment (125). There was evidence that a small group of women stopped drinking at the time of diagnosis, possibly due to information regarding an alcohol-breast cancer association. This may have led to recall bias by these women if they tended to underreport past or recent intake. However, removal of their data from analyses did not appear to meaningfully alter estimates. Although other studies have detected an increased risk for former drinkers compared with nondrinkers (117, 126), this may be primarily a reflection of time since cessation of alcohol intake.

Biological data suggest that high alcohol intake may increase breast cancer risk by one of several mechanisms: producing a direct mitogenic effect on breast tissues; increasing serum concentrations of estrogens by either an effect on hepatic or pituitary-gonadal function; or, acting as a cocarcinogen (37, 38, 127, 128). At present, most data support the hypothesis that alcohol increases circulating concentrations of estrogens. The association between alcohol and hormone levels is not straightforward. Several observational studies have reported that alcohol intake is associated with increased plasma or urinary estrogens in postmenopausal women (91, 129-131). However, it has also been reported that acute alcohol ingestion increases blood estrogens only in postmenopausal women who are taking estrogen replacement therapy (38). Dorgan et al. (132) did not find an association between alcohol intake and plasma estrogens in premenopausal women across the menstrual cycle. Reichman et al. (37), however, reported that an alcohol dose of 30 g/day increased estrogen concentrations in a controlled, randomized trial in premenopausal women. Most investigations have been based on small, volunteer samples of women, and in such studies it is difficult to account for binge drinking, variability in alcohol metabolism, and alcohol-plasma hormone levels over several menstrual cycles (132).

A mechanism whereby a low alcohol intake might decrease risk is unknown at this time. The presence of this finding for both premenopausal and postmenopausal non-Hispanic white women seems to argue against an effect mediated by a change in hormone level. Whatever the explanation may be, whether real or spurious, the present study is not the only one to find a potential protective effect for light to moderate alcohol consumption. Longnecker et al.'s (13) study of alcohol consumption among postmenopausal women showed evidence for a modest protective effect associated with lifetime alcohol intake at low levels (OR=0.88 95 percent CI 0.67-1.15 for >0-5 g/day; OR=0.70 95 percent CI 0.51-0.94 for 6-11 g/day). Only a few other studies have reported a protective effect associated with a low alcohol level, and these have varied depending on menopausal status (120, 133, 134).

In conclusion, the results of the present study indicate that alcohol intake is not a risk factor for breast cancer in New Mexico Hispanic women. It does not seem likely that alcohol intake explains the increasing incidence of breast cancer in New Mexico Hispanic women, because there appears to be no consistent relationship in the low to moderate range observed, and high alcohol intake is rare. More research is needed to determine whether the reduced risk for

low intake can be replicated in other studies, or is an artifact due to bias or unmeasured confounders in the present study.

Table 1. Participant characteristics, stratified by ethnicity and case-control status, New Mexico Women's Health Study, 1992-1994

	Hispanic				non-Hispanic White			
	Cases (n=332)		Controls (n=388)		Cases (n=380)		Controls (n=456)	
	No. *	%	No.	%	No.	%	No.	%
Age group (years)								
30-39	42	12.7	55	14.2	33	8.7	67	14.7
40-64	221	66.6	255	65.7	275	72.4	290	63.6
65-74	69	20.8	78	20.1	72	18.9	99	21.7
Education (years)								
< 12	104	31.3	86	22.2	24	6.3	29	6.4
12	129	38.9	150	38.7	102	26.8	111	24.3
> 12	96	28.9	152	39.2	253	66.6	315	69.1
Missing	3	0.9	1	0.3	1	0.3	1	0.2
Income								
<= $9,999	78	23.5	51	13.1	22	5.8	24	5.3
$10,000-$19,000	81	24.4	83	21.4	47	12.4	66	14.5
$20,000-$29,000	53	16.0	67	17.3	73	19.2	75	16.4
$30,000-$39,000	48	14.5	64	16.5	52	13.7	75	16.4
>= $40,000	55	16.6	112	28.9	167	43.9	204	44.7
Missing	17	5.1	11	2.8	19	5.0	12	2.6
Marital status								
Ever-married	308	92.8	365	94.1	360	94.7	438	96.1
Never-married	24	7.2	23	5.9	20	5.3	18	3.9
Age (years) at menarche								
<= 12	133	40.1	170	43.8	185	48.7	211	46.3
13	101	30.4	109	28.1	111	29.2	140	30.7
>= 14	95	28.6	108	27.8	84	22.1	103	22.6
Missing	3	0.9	1	0.3	0	0.0	2	0.4
Age (years) at first full-term birth								
<= 18	71	21.4	89	22.9	43	11.3	67	14.7
19-20	71	21.4	94	24.2	60	15.8	73	16.0
21-22	50	15.1	64	16.5	59	15.5	64	14.0
23-26	62	18.7	68	17.5	82	21.6	95	20.8
>= 27	40	12.0	43	11.1	76	20.0	84	18.4
Nulliparous	38	11.4	30	7.7	60	15.8	73	16.0

Table 1. (Continued)

	Hispanic				non-Hispanic White			
	Cases		Controls		Cases		Controls	
	(n=332)	%	(n=388)	%	(n=380)	%	(n=456)	%
	No. *		No.		No.		No.	
Number of full-term births								
Nulliparous	38	11.4	30	7.7	60	15.8	73	16.0
1	29	8.7	35	9.0	63	16.6	58	12.7
2	66	19.9	98	25.3	128	33.7	138	30.3
3	80	24.1	72	18.6	66	17.4	101	22.1
>= 4	119	35.8	153	39.4	63	16.6	86	18.9
Cumulative months of lactation								
Nulliparous	38	11.4	30	7.7	60	15.8	73	16.0
Parous, 1-12 months	109	32.8	128	33.0	167	43.9	157	34.4
Parous, >12 months	52	15.7	82	21.1	43	11.3	99	21.7
Parous, never	133	40.1	145	37.4	110	28.9	125	27.4
Missing	0	0.0	3	0.8	0	0.0	2	0.4
Cumulative years of oral contraceptive use								
Never used	149	44.9	146	37.6	146	38.4	155	34.0
< 1.5	59	17.8	82	21.1	80	21.1	67	14.7
1.5 - 5	54	16.3	75	19.3	67	17.6	114	25.0
> 5	67	20.2	84	21.6	83	21.8	118	25.9
Missing	3	0.9	1	0.3	4	1.1	2	0.4
Menopausal status † (based on coding shown below)								
Pre-menopausal	131	39.5	154	39.7	116	30.5	186	40.8
Post-menopausal	178	53.6	219	56.4	239	62.9	249	54.6
Surgical unknown	21	6.3	14	3.6	24	6.3	21	4.6
Unknown	2	0.6	1	0.3	1	0.3	0	0.0
Menopausal status								
Pre-menopausal	120	36.1	148	38.1	110	28.9	176	38.6
Post-natural menopause	97	29.2	101	26.0	145	38.2	131	28.7
Post-surgical menopause	50	15.1	76	19.6	71	18.7	94	20.6
Surgical unknown	21	6.3	14	3.6	24	6.3	21	4.6
Surgical Unknown, < age 44	11	3.3	6	1.5	6	1.6	10	2.2
Surgical Unknown > age 54	31	9.3	42	10.8	23	6.1	24	5.3
Unknown	2	0.6	1	0.3	1	0.3	0	0.0

Table 1. (Continued)

	Hispanic				non-Hispanic White			
	Cases		Controls		Cases		Controls	
	(n=332)	%	(n=388)	%	(n=380)	%	(n=456)	%
	No. *		No.		No.		No.	
Age (years) at natural menopause								
<= 44	19	19.6	19	18.8	24	16.6	22	16.8
45-49	41	42.3	41	40.6	44	30.3	45	34.4
50-51	26	26.8	24	23.8	43	29.7	31	23.7
>= 52	11	11.3	17	16.8	34	23.4	33	25.2
Estrogen use								
Yes	112	33.7	163	42.0	200	52.6	214	46.9
No	218	65.7	224	57.7	180	47.4	239	52.4
Missing	2	0.6	1	0.3	0	0.0	3	0.7
History of fibrocystic disease								
Yes	45	13.6	40	10.3	95	25.0	77	16.9
No	274	82.5	348	89.7	268	70.5	375	82.2
Missing	13	3.9	0	0.0	17	4.5	4	0.9
Body mass index (kg/m^2) ‡								
< 21.1	35	10.5	75	19.3	119	31.3	134	29.4
21.1 - <23.0	65	19.6	73	18.8	126	33.2	132	28.9
23.0 - <25.6	95	28.6	109	28.1	68	17.9	103	22.6
>= 25.6	133	40.1	124	32.0	65	17.1	85	18.6
Missing	4	1.2	7	1.8	2	0.5	2	0.4
Cigarette smoking								
Yes	145	43.7	186	47.9	185	48.7	240	52.6
No	187	56.3	202	52.1	195	51.3	216	47.4
Breast cancer in mother, sister, daughter								
No	292	88.0	352	90.7	317	83.4	402	88.2
Yes	40	12.0	36	9.3	63	16.6	54	11.8

Table 1. (Continued)

	Hispanic				non-Hispanic White			
	Cases		Controls		Cases		Controls	
	(n=332)	%	(n=388)	%	(n=380)	%	(n=456)	%
	No. *		No.		No.		No.	
Vigorous physical activity (METS/ week) §								
None/non-vigorous	148	44.6	106	27.3	108	28.4	87	19.1
Light, <13	92	27.7	110	28.4	95	25.0	142	31.1
Moderate, 13 - <35	47	14.2	76	19.6	104	27.4	118	25.9
Heavy , >= 35	45	13.6	96	24.7	73	19.2	109	23.9
Energy intake (kilocalories/day)								
< 1608	68	20.5	87	22.4	105	27.6	79	17.3
1608 - <2018	59	17.8	58	14.9	86	22.6	108	23.7
2019 - <2436	72	21.7	71	18.3	68	17.9	95	20.8
2436 - <3032	56	16.9	79	20.4	59	15.5	87	19.1
>= 3032	71	21.4	84	21.6	59	15.5	82	18.0
Missing	6	1.8	9	2.3	3	0.8	5	1.1
Total fat intake (grams/day) ¶								
< 58	75	22.6	80	20.6	106	27.9	86	18.9
58 - <75	64	19.3	62	16.0	89	23.4	104	22.8
75 - <96	63	19.0	78	20.1	67	17.6	88	19.3
96 - <123	57	17.2	82	21.1	53	13.9	84	18.4
>= 123	67	20.2	77	19.8	62	16.3	89	19.5
Missing	6	1.8	9	2.3	3	0.8	5	1.1

* Numbers (No.) may not sum to total for all variables because of missing data. Percentages (%) based on total for each category.

† Premenopausal includes: pre-menopausal and surgical unknown (age <10th percentile or <= 43 yrs).
Post-menopausal includes: post-natural menopause, surgical menopause, and surgical unknowns (age >90th percentile or >=54 yrs).

‡ kg/m^2, kilograms/meters squared.

§ METS, metabolic equivalents, based on expenditure of kilocalories/kilogram of weight/hour. Physical activities included: walking/hiking, running/jogging, exercise class, biking, dancing, lap swimming, tennis, squash/racquetball, calisthenics/rowing, bowling, golf, softball/baseball, basketball, volleyball, housework, and heavy outside work.

¶ Absolute intake.

Table 2. Ever *vs.* never alcohol consumption and alcohol usage patterns, stratified by ethnicity and case-control status, New Mexico Women's Health Study, 1992-1994

	Hispanic				non-Hispanic White			
	Cases		Controls		Cases		Controls	
	No.	%	No.	%	No.	%	No.	%
History of alcohol consumption								
Never	83	25.0	82	21.1	51	13.4	46	10.1
Ever	249	75.0	306	78.9	329	86.6	410	89.9
Status of alcohol consumption at interview								
Nondrinker	83	25.0	82	21.1	51	13.4	46	10.1
Current drinker	166	50.0	230	59.3	233	61.3	328	71.9
Former drinker	83	25.0	76	19.6	96	25.3	82	18.0
Age (years) at first alcohol use								
Nondrinker	83	25.0	82	21.1	51	13.4	46	10.1
<= 16	40	12.0	63	16.2	72	18.9	120	26.3
17 - 18	47	14.2	70	18.0	94	24.7	117	25.7
19 - 21	72	21.7	88	22.7	95	25.0	102	22.4
>= 22	90	27.1	85	21.9	68	17.9	71	15.6
Years since last alcohol consumption *†								
Nondrinker	83	25.0	82	21.1	51	13.4	46	10.1
Stopped within reference year	21	6.3	2	0.5	23	6.1	3	0.7
1	7	2.1	4	1.0	9	2.4	3	0.7
2-4	11	3.3	7	1.8	13	3.4	10	2.2
5-14	18	5.4	14	3.6	24	6.3	32	7.0
>= 15	25	7.5	48	12.4	27	7.1	34	7.5
Current drinker	166	50.0	230	59.3	233	61.3	328	71.9
Duration (years) of drinking *†								
Nondrinker	83	25.3	82	21.1	52	13.7	46	10.1
< 10	20	6.0	32	8.2	16	4.2	21	4.6
10 - 39	201	60.5	224	57.7	230	60.5	286	62.7
>= 40	27	8.1	49	12.6	82	21.6	103	22.6

* Age when alcohol consumption stopped was missing for 1 case and 1 control.

† Does not reflect actual duration of drinking; based on reported age at cessation or reference age minus first age of alcohol use.

TABLE 3. Frequency of intake at ages 25, 35, and 50, stratified by ethnicity and case-control status, New Mexico Women's Health Study, 1992-1994

	Hispanic				non-Hispanic White			
	Cases		Controls		Cases		Controls	
	No.	% *	No.	%	No.	%	No.	%
Alcohol intake, age 25								
Nondrinkers	83	25.0	82	21.1	51	13.4	46	10.1
Current drinkers	186	56.0	229	59.0	268	70.5	334	73.2
Drank at other times	63	19.0	77	19.8	61	16.1	76	16.7
Frequency of drinking, age 25†								
Daily	3	1.6	10	4.4	27	7.1	22	6.6
Weekly	53	28.5	61	26.6	91	23.9	146	43.7
Monthly	66	35.5	79	34.5	78	20.5	94	28.1
Yearly	64	34.4	79	34.5	72	18.9	72	21.6
Alcohol intake, age 35 ‡								
Nondrinkers	83	26.2	79	21.9	50	13.5	45	10.6
Current drinkers	188	59.3	218	60.4	270	72.8	315	73.9
Drank at other times	46	14.5	64	17.7	51	13.7	66	15.5
Unexposed, reference age <35	15	---	27	---	9	---	30	---
Frequency of drinking, age 35 †								
Daily	5	2.7	16	7.3	36	13.3	25	7.9
Weekly	57	30.3	57	26.1	101	37.4	136	43.2
Monthly	59	31.4	70	32.1	69	25.6	97	30.8
Yearly	67	35.6	75	34.4	64	23.7	57	18.1
Alcohol intake, age 50 ‡								
Nondrinkers	59	31.9	60	28.7	44	16.9	33	13.8
Current drinkers	94	50.8	102	48.8	170	65.1	171	71.3
Drank at other times	32	17.3	47	22.5	47	18.0	36	15.0
Unexposed, reference age <50	147	---	179	---	119	---	216	---
Frequency of drinking, age 50 †								
Daily	5	5.3	7	6.9	34	20.0	37	21.6
Weekly	23	24.5	32	31.4	59	34.7	61	35.7
Monthly	29	30.9	28	27.5	36	21.2	39	22.8
Yearly	37	39.4	35	34.3	41	24.1	34	19.9

* Percentages (%) based on total for each category.

† Includes only subjects who reported alcohol intake; 'Current drinkers', at 25, 35, or 50.

‡ Percentages (%) based on total number of women whose reference age was equal to, or greater than the age at alcohol intake (excludes 'Unexposed, reference age').

Table 4. Lifetime alcohol consumption based on reported intake at ages 25 to 50 years, and recent alcohol intake based on a food frequency questionnaire, stratified by ethnicity and case-control status, New Mexico Women's Health Study, 1992-1994

	Hispanic				non-Hispanic White			
	Cases		Controls		Cases		Controls	
	No.	%	No.	%	No.	%*	No.	%
Average lifetime gram intake/week (based on alcohol intake at age 25,35, or 50) †								
Nondrinkers	83	25.0	82	21.1	51	13.4	46	10.1
<= 8	131	39.5	157	40.5	116	30.5	132	29.0
8 - <21 (1 drink)	31	9.3	37	9.5	50	13.2	63	13.8
21- <42 (2 drinks)	32	9.6	40	10.3	36	9.5	58	12.7
42- <84 (3-4 drinks)	19	5.7	23	5.9	57	15.0	70	15.4
84 - <148 (5-7 drinks)	13	3.9	18	4.6	32	8.4	29	6.4
>=148 (8+drinks)	10	3.0	10	2.6	27	7.1	39	8.6
Drank at other times	13	3.9	21	5.4	11	2.9	19	4.2
Recent alcohol intake (grams/week) †‡§								
Nondrinker ¶	212	63.9	236	60.8	189	49.7	188	41.2
<= 8	33	10.0	43	11.1	34	9.0	47	10.3
8 - <21 (1 drink)	28	8.4	38	9.8	33	8.7	57	12.5
21- <42 (2 drinks)	22	6.6	29	7.5	31	8.2	54	11.8
42- <84 (3-4 drinks)	13	3.9	15	3.9	35	9.2	49	10.8
84 - <148 (5-7 drinks)	18	5.4	18	4.6	17	4.5	29	6.4
>=148 (8+ drinks)	0	0.0	0	0.0	38	10.0	27	5.9
Missing	6	1.8	9	2.3	3	0.8	5	1.1

* Absolute intake.

† Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

‡ No intake in four-week period, six months in past.

TABLE 5. Age-adjusted odds ratios (OR) and 95% confidence intervals (CI) for risk factors of breast cancer, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994 *

Risk Factor	Hispanic				non-Hispanic White			
	Cases	Controls			Cases	Controls		
	No. †	No.	OR	95%CI	No.	No.	OR	95%CI
Education (years)								
< 12	104	86	1.47	0.99-2.18	24	29	0.89	0.48-1.64
12	129	150	1.00		102	111	1.00	
> 12	96	152	0.68	0.47-0.97	253	315	0.89	0.64-1.25
Age (years) at menarche								
<= 12	133	170	0.88	0.60-1.28	185	211	1.15	0.80-1.64
13	101	109	1.08	0.72-1.61	111	140	1.03	0.70-1.53
>= 14	95	108	1.00		84	103	1.00	
Age (years) at first full-term birth								
<= 18	71	89	1.00		43	67	1.00	
19-20	71	94	1.02	0.65-1.59	60	73	1.19	0.71-2.01
21-22	50	64	1.04	0.64-1.71	59	64	1.32	0.77-2.45
23-26	62	68	1.14	0.70-1.84	82	95	1.33	0.81-2.18
>= 27	40	43	1.23	0.71-2.13	76	84	1.56	0.94-2.60
Nulliparous	38	30	1.54	0.85-2.77	60	73	1.30	0.77-2.22
Number of full-term births								
Nulliparous	38	30	1.46	0.83-2.57	60	73	1.33	0.81-2.19
1	29	35	0.99	0.55-1.79	63	58	1.90	1.13-3.17
2	66	98	0.78	0.51-1.20	128	138	1.56	1.02-2.40
3	80	72	1.43	0.93-2.18	66	101	0.94	0.59-1.50
>= 4	119	153	1.00		63	86	1.00	
Cumulative months of lactation								
Nulliparous	38	30	1.30	0.75-2.26	60	73	0.96	0.62-1.51
Parous, 1-12	109	128	0.93	0.65-1.34	167	157	1.24	0.88-1.76
Parous, >12	52	82	0.68	0.44-1.06	43	99	0.53	0.34-0.84
Parous, never	133	145	1.00		110	125	1.00	
Cumulative years of oral contraceptive use								
Never used	149	146	1.00		146	155	1.00	
< 1.5	59	82	0.71	0.46-1.09	80	67	1.32	0.85-2.06
1.5 - 5	54	75	0.61	0.38-0.98	67	114	0.76	0.48-1.19
> 5	67	84	0.70	0.45-1.09	83	118	0.86	0.56-1.32
Menopausal status ‡								
Premenopausal	131	154	1.00		116	186	1.00	
Postmenopausal	178	219	1.18	0.67-2.08	239	249	0.86	0.51-1.48
Surgical Unknown	21	14	1.80	0.85-3.80	24	21	1.43	0.74-2.78

Table 5. (Continued)

Risk Factor	Hispanic				non-Hispanic White			
	Cases	Controls			Cases	Controls		
	No. †	No.	OR	95%CI	No.	No.	OR	95%CI
History of fibrocystic disease								
No	287	348	1.00		285	379	1.00	
Yes	45	40	1.31	0.83-2.09	95	77	1.68	1.18-2.39
Breast cancer in mother, sister, daughter								
No	292	352	1.00		317	402	1.00	
Yes	40	36	1.30	0.80-2.12	63	54	1.46	0.98-2.18
Cigarette smoking								
No	187	202	1.00		195	216	1.00	
Yes	145	186	0.84	0.62-1.14	185	240	0.84	0.63-1.11
Body mass index (kg/m^2) §								
< 21.1	35	75	1.00		119	134	1.00	
21.1 - <23.0	65	73	1.88	1.11-3.20	126	132	1.05	0.73-1.50
23.0 - <25.6	95	109	1.87	1.14-3.06	68	103	0.65	0.43-0.97
>= 25.6	133	124	2.38	1.46-3.87	65	85	0.81	0.53-1.24
Vigorous physical activity (METS/ week) ¶								
None/non-vigorous	148	106	1.00		108	87	1.00	
Light, <13	92	110	0.62	0.42-0.90	95	142	0.55	0.37-0.81
Moderate, 13 - <35	47	76	0.45	0.29-0.71	104	118	0.73	0.49-1.08
Heavy , >= 35	45	96	0.34	0.22-0.54	73	109	0.55	0.36-0.84
Energy intake (kilocalories/day)								
< 1608	68	87	1.00		105	79	1.00	
1608 - <2018	59	58	1.27	0.78-2.07	86	108	0.60	0.39-0.90
2019 - <2436	72	71	1.37	0.86-2.20	68	95	0.54	0.35-0.84
2436 - <3032	56	79	0.95	0.59-1.53	59	87	0.52	0.33-0.82
>= 3032	71	84	1.08	0.68-1.71	59	82	0.55	0.35-0.87
Total fat intake (grams/day) #								
< 58	75	80	1.00		106	86	1.00	
58 - <75	64	62	1.09	0.68-1.76	89	104	0.67	0.44-1.01
75 - <96	63	78	0.86	0.54-1.37	67	88	0.66	0.42-1.02
96 - <123	57	82	0.78	0.49-1.26	53	84	0.53	0.34-0.85
>= 123	67	77	0.92	0.57-1.46	62	89	0.57	0.37-0.89

Table 5. (Continued)

* Conditional logistic regression models matched for age-group, and health planning district, and additionally adjusted for age.

† Numbers (No.) may not sum to total for all covariates because of missing data.

‡ Premenopausal includes: pre-menopausal and surgical unknown (age <10th percentile or <= 43 yrs).

Post-menopausal includes: post-natural menopause, surgical menopause, and surgical unknowns (age >90th percentile or >=54 yrs).

§ kg/m^2, kilograms/meters squared.

¶ METS, metabolic equivalents, based on expenditure of kilocalories/kilogram of weight/hour. Physical activities included: walking/hiking, running/jogging, exercise class, biking, dancing, lap swimming, tennis, squash/racquetball, calisthenics/rowing, bowling, golf, softball/baseball, basketball, volleyball, housework, and heavy outside work.

Absolute intake

TABLE 6. Odds ratios (OR) and 95% confidence intervals (CI) for age-adjusted models, and multivariate-adjusted full models for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

Alcohol Exposure Variable	Hispanic						non-Hispanic White					
	Cases	Controls	Age-adjusted *		Full †		Cases	Controls	Age-adjusted		Full	
	No.	No.	OR	95%CI	OR	95%CI	No.	No.	OR	95%CI	OR	95%CI
Recent alcohol intake (grams/week) ‡§¶												
Nondrinker #	212	236	1.00		1.00		189	188	1.00		1.00	
< 8	33	43	0.89	0.54-1.47	1.21	0.68-2.15	34	47	0.71	0.43-1.16	0.49	0.28-0.85
8 - <21 (1 drink)	28	38	0.77	0.45-1.32	1.00	0.54-1.85	33	57	0.57	0.35-0.93	0.46	0.27-0.79
21 - <42 (2 drinks)	22	29	0.80	0.44-1.47	0.75	0.37-1.53	31	54	0.60	0.36-1.00	0.44	0.25-0.77
42 - <85 (3-4 drinks)	13	15	0.95	0.44-2.06	1.24	0.52-2.93	35	49	0.71	0.43-1.16	0.60	0.35-1.05
85 - <148 (5-7 drinks)	18	18	1.14	0.57-2.29	1.35	0.63-2.93	17	29	0.58	0.30-1.12	0.49	0.24-1.00
>= 148 (8+ drinks)	0	0					38	27	1.42	0.82-2.46	1.56	0.85-2.86

* Conditional logistic regression models matched for age-group, and health planning district, and additionally adjusted for age.

† Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, vigorous physical activity, energy intake, and energy-adjusted total fat intake.

‡ Absolute intake.

§ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

¶ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.

No intake in four-week period, six months in past.

TABLE 7. Covariates with 10 percent or greater change-in-estimate (odds ratio) for recent alcohol intake, based on a food frequency questionnaire, and average lifetime intake based on ages 25, 35, and 50, New Mexico Women's Health Study, 1992-1994 *

Covariate	Alcohol Exposure Variable	Hispanic			non-Hispanic White		
		Menopausal Status			Menopausal Status		
		All	Pre †	Post †	All	Pre	Post
Education	Recent	19	36	61	-	-	12
	Average lifetime	16	49	10	-	-	15
Age (years) at menarche	Recent	-	-	-25	-	-	10
	Average lifetime	-	19	-	-	-	-
Age (years) at first full-term birth	Recent	11	24	-	-	-	-11
	Average lifetime	-	23	-12	-	17	13
Number of full-term births	Recent	-	-	44	-	-	-11
	Average lifetime	12	39	10	-	-16	-15
Cumulative months of lactation	Recent	-	28	-	-	-	-
	Average lifetime	-	-21	-	-	-	-14
Cumulative years oral contraceptive use	Recent	-	25	35	-	-	-
	Average lifetime	16	33	16	-	-10	14
History of fibrocystic disease	Recent	-	-10	-15	-	-	-
	Average lifetime	-	-16	-	-	-	-
Breast cancer in mother, sister, daughter	Recent	-	-	-32	-	-	-
	Average lifetime	-	11	-	-	-	-
Cigarette smoking	Recent	-	-	-	10	-	38
	Average lifetime	13	-	12	-	-	27
Body mass index (kg/m^2) ‡	Recent	13	-	20	-	-25	19
	Average lifetime	-13	-64	10	-	-19	-
Vigorous physical activity (METS/week) §	Recent	-10	25	36	-	-	19
	Average lifetime	-	28	-24	-	21	-

Table 7. (Continued)

Covariate	Alcohol Exposure Variable	Hispanic			non-Hispanic White		
		Menopausal Status			Menopausal Status		
		All	Pre †	Post †	All	Pre	Post
Energy intake (kilocalories/week)	Recent	-	-	20	16	-	34
	Average lifetime	11	-	-	-	-	-
Energy-adjusted total fat (grams/week)	Recent	-	-	27	-	-	-
	Average lifetime	-	-21	-	-	-11	-

* Change in estimate (odds ratio) <10 percent noted as '-'.
† Pre, premenopausal; Post, postmenopausal.
‡ kg/m^2, kilograms/meters squared.
§ METS, metabolic equivalents, based on expenditure of kilocalories/kilogram of weight/hour.

TABLE 8. Odds ratios (OR) and 95% confidence intervals (CI) for reduced models for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

Alcohol Exposure Variable	Hispanic Reduced Model * OR	Hispanic Reduced Model * 95%CI	non-Hispanic White Reduced Model † OR	non-Hispanic White Reduced Model † 95%CI
Recent alcohol intake (grams/week) ‡§¶				
Nondrinker #	1.00		1.00	
< 8	1.28	0.72-2.25	0.65	0.39-1.08
8 - <21 (1 drink)	1.02	0.55-1.88	0.49	0.30-0.82
21 - <42 (2 drinks)	0.80	0.39-1.60	0.56	0.34-0.95
42 - <85 (3-4 drinks)	1.20	0.51-2.82	0.72	0.43-1.20
85 - <148 (5-7 drinks)	1.24	0.58-2.68	0.65	0.33-1.26
>= 148 (8+ drinks)			1.65	0.93-2.92

* Conditional logistic regression models matched for age-group and health planning district, and adjusted for all variables except for fibrocystic disease and cigarette smoking.

† Conditional logistic regression models matched for age-group and health planning district, and adjusted for age, energy intake, cigarette smoking, and body mass index.

‡ Absolute intake.

§ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

¶ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.

\# No intake in four-week period, six months in past.

TABLE 9. Odds ratios (OR) and 95% confidence intervals (CI) for age-adjusted models, multivariate-adjusted full models and reduced models for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity and menopausal status, New Mexico Women's Health Study, 1992-1994 *

	Premenopausal Status											
	Hispanic						non-Hispanic White					
Alcohol Exposure Variable	Age-adjusted *		Full †		Reduced ‡		Age-adjusted *		Full †		Reduced §	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Recent alcohol intake (grams/week) ¶#**												
Nondrinker ‡‡	1.00		1.00		1.00		1.00		1.00		1.00	
< 8	1.21	0.57-2.58	1.68	0.66-4.26	1.71	0.68-4.32	0.66	0.27-1.62	0.29	0.10-0.87	0.54	0.21-1.38
8 - <21 (1 drink)	0.73	0.33-1.61	0.64	0.24-1.71	0.64	0.24-1.72	0.33	0.15-0.71	0.24	0.09-0.61	0.30	0.13-0.67
21 - <42 (2 drinks)	1.02	0.44-2.35	0.78	0.26-2.32	0.81	0.28-2.31	0.48	0.23-1.02	0.28	0.11-0.75	0.43	0.19-0.95
42 - <85 (3-4 drinks)	1.28	0.43-3.82	1.68	0.43-6.47	1.76	0.48-6.48	0.60	0.26-1.38	0.40	0.14-1.14	0.59	0.25-1.41
85 - <148 (5-7 drinks)	0.65	0.22-1.86	0.61	0.16-2.25	0.54	0.15-1.96	0.58	0.18-1.88	0.29	0.07-1.17	0.64	0.19-2.15
>= 148 (8+ drinks)							1.24	0.45-3.43	1.08	0.32-3.68	1.04	0.36-3.02
	Postmenopausal Status											
Recent alcohol intake (grams/week) ¶#**												
Nondrinker ‡‡	1.00		1.00		1.00		1.00		1.00		1.00	
< 8	0.69	0.34-1.40	0.93	0.38-2.26	0.93	0.39-2.22	0.67	0.35-1.27	0.59	0.28-1.22	0.64	0.33-1.24
8 - <21 (1 drink)	0.83	0.36-1.87	1.47	0.55-3.92	1.54	0.58-4.09	0.92	0.46-1.83	0.63	0.29-1.37	0.72	0.35-1.48
21 - <42 (2 drinks)	0.49	0.17-1.42	0.43	0.12-1.62	0.52	0.14-1.93	0.45	0.20-1.01	0.36	0.15-0.92	0.42	0.18-0.97
42 - <85 (3-4 drinks)	0.65	0.18-2.33	0.83	0.21-3.35	0.73	0.18-2.93	0.81	0.42-1.55	0.67	0.31-1.44	0.85	0.43-1.66
85 - <148 (5-7 drinks)	2.54	0.89-7.27	4.25	1.18-15.3	4.23	1.15-15.6	0.61	0.28-1.33	0.54	0.22-1.34	0.73	0.32-1.62
>= 148 (8+ drinks)							1.53	0.76-3.09	2.23	0.98-5.05	2.17	1.03-4.58

Table 9. (Continued)

* Conditional logistic regression models matched for age-group and health planning district, and adjusted additionally for age.
† Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.
‡ Conditional logistic regression models matched for age-group and health planning district, and adjusted for all variables except for fibrocystic disease and cigarette smoking.
§ Conditional logistic regression models matched for age-group and health planning district, and adjusted for age, energy intake, cigarette smoking, and body mass index.
¶ Absolute intake.
# Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.
** Recent alcohol intake data missing or excluded for 9 cases and 14 controls.
‡‡ No intake in four-week period, six months in past.

TABLE 10. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with recent alcohol intake, collapsed into fewer categories, based on a food frequency questionnaire, stratified by ethnicity and menopausal status, New Mexico Women's Health Study, 1992-1994 *

	Hispanic - Recent Alcohol Intake †					
	Low		Medium		High	
	OR	95%CI	OR	95%CI	OR	95%CI
Nondrinker	1.00		1.00		1.00	
All §	1.21	0.68-2.15	0.88	0.54-1.45	1.31	0.72-2.38
Premenopausal	1.69	0.67-4.30	0.70	0.32-1.51	0.96	0.36-2.60
Postmenopausal	0.89	0.37-2.14	0.96	0.42-2.18	2.03	0.81-5.09

	non-Hispanic White - Recent Alcohol Intake ‡			
	Low		High	
	OR	95%CI	OR	95%CI
Nondrinker	1.00		1.00	
All §	0.49	0.35-0.69	1.55	0.84-2.83
Premenopausal	0.29	0.15-0.56	1.08	0.32-3.64
Postmenopausal	0.56	0.35-0.90	2.23	0.99-5.03

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Hispanic, levels of recent alcohol intake (grams/week): Low=<8 (<1 drink); Medium=8-<42 (1-2 drinks); High=42+ (3+ drinks).

‡ non-Hispanic White, levels of recent alcohol intake (grams/week): Low=<148 (<8 drinks); High=148+ (8+ drinks).

§ Menopausal status included in these models.

Table 11. Distribution of hormone receptor status for breast cancer cases, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

	Hispanic		non-Hispanic White	
	No.	%	No.	%
Hormone receptor status				
None done	50	15.06	58	15.26
ER+/PR+	130	39.16	156	41.05
ER-/PR-	79	23.80	65	17.11
ER-/PR+	9	2.71	11	2.89
ER+/PR-	33	9.94	44	11.58
Unknown*	31	9.34	46	12.11

* Includes "borderline" for either ER or PR receptor; and one or both hormone receptors unknown.

TABLE 12. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity and joint estrogen/progesterone receptor status, New Mexico Women's Health Study, 1992-1994 *

	Controls	ER+PR+			ER-PR-		
Alcohol Exposure Variable	**No. †**	**No.**	**OR**	**95%CI**	**No.**	**OR**	**95%CI**
Hispanic							
Recent alcohol intake (grams/week) ‡							
Nondrinker	236	80	1.00		50	1.00	
< 8	43	10	0.83	0.35-1.98	9	1.04	0.39-2.79
8 - <42 (1-2 drinks)	67	20	0.97	0.49-1.91	7	0.39	0.14-1.08
>= 42 (3+ drinks)	33	18	1.78	0.86-3.68	9	1.43	0.55-3.74
non-Hispanic White							
Recent alcohol intake (grams/week) ‡							
Nondrinker	188	72	1.00		33	1.00	
< 148 (<8 drinks)	236	59	0.46	0.28-0.74	27	0.37	0.19-0.73
>= 148 (8+ drinks)	27	22	2.13	1.03-4.43	5	1.62	0.51-5.18

* Polytomous logistic regression models matched for age-group, and health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Recent alcohol intake data missing for 14 controls, 5 cases with ES+PR+ status breast cancer, and 4 cases with ES-PR- status breast cancer. The remaining cases were categorized as: ES+PR- (77), ES-PR+ (20); hormone-receptor determination not done (108); and either results borderline or unknown (77).

‡ Absolute intake.

TABLE 13. Odds ratios (OR) and 95% confidence intervals (CI) for age-adjusted models, and multivariate-adjusted full models for breast cancer risk associated with ever *vs.* never alcohol consumption and alcohol usage patterns, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

Alcohol Exposure Variable	Hispanic						non-Hispanic White					
	Cases	Controls	Age-adjusted *		Full †		Cases	Controls	Age-adjusted *		Full †	
	No.	No.	OR	95%CI	OR	95%CI	No.	No.	OR	95%CI	OR	95%CI
History of alcohol consumption												
Never	83	82	1.00		1.00		51	46	1.00		1.00	
Ever	249	306	0.78	0.54-1.14	0.96	0.61-1.50	329	410	0.76	0.49-1.19	0.72	0.43-1.19
Status of alcohol consumption at interview												
Nondrinker	83	82	1.00		1.00		51	46	1.00		1.00	
Current drinker	166	230	0.69	0.46-1.02	0.84	0.52-1.36	233	328	0.67	0.43-1.06	0.60	0.36-1.01
Former drinker	83	76	1.03	0.65-1.61	1.21	0.71-2.05	96	82	1.08	0.65-1.81	1.09	0.61-1.95
Years since last alcohol consumption ‡												
Nondrinker	83	82	1.00		1.00		51	46	1.00		1.00	
Stopped w/in reference year	21	2	12.13	2.51-58.6	12.13	2.51-58.6	23	3	8.04	2.03-31.7	8.04	2.03-31.7
1	7	4	2.77	0.57-13.5	2.77	0.57-13.5	9	3	2.10	0.48-9.23	2.10	0.48-9.23
2-4	11	7	1.86	0.58-5.95	1.86	0.58-5.95	13	10	1.57	0.54-4.55	1.57	0.54-4.55
5-14	18	14	1.65	0.67-4.05	1.65	0.67-4.05	24	32	0.78	0.36-1.66	0.78	0.36-1.66
>= 15	25	48	0.53	0.27-1.03	0.53	0.27-1.03	27	34	0.64	0.30-1.35	0.64	0.30-1.35
Current drinker	166	230	0.90	0.56-1.46	0.90	0.56-1.46	233	328	0.62	0.37-1.05	0.62	0.37-1.05
Age (years) at first alcohol use												
Nondrinker	83	82	1.00		1.00		51	46	1.00		1.00	
<= 16	40	63	0.71	0.37-1.36	0.71	0.37-1.36	72	120	0.61	0.33-1.12	0.61	0.33-1.12
17 - 18	47	70	0.67	0.36-1.23	0.67	0.36-1.23	94	117	0.67	0.37-1.20	0.67	0.37-1.20
19 - 21	72	88	0.95	0.55-1.65	0.95	0.55-1.65	95	102	0.80	0.46-1.42	0.80	0.46-1.42
>= 22	90	85	1.21	0.72-2.03	1.21	0.72-2.03	68	71	0.73	0.40-1.32	0.73	0.40-1.32

Table 13. (Continued)

Alcohol Exposure Variable	Hispanic						non-Hispanic White					
	Cases	Controls	Age-adjusted *		Full †		Cases	Controls	Age-adjusted *		Full †	
	No.	No.	OR	95%CI	OR	95%CI	No.	No.	OR	95%CI	OR	95%CI
Duration (years) of drinking ‡§												
Nondrinker	83	82	1.00		1.00		52	46	1.00		1.00	
< 10	20	32	0.82	0.39-1.70	0.82	0.39-1.70	16	21	0.69	0.29-1.64	0.69	0.29-1.64
10 - 39	201	224	1.06	0.66-1.73	1.06	0.66-1.73	230	286	0.80	0.47-1.37	0.80	0.47-1.37
>= 40	27	49	0.76	0.37-1.57	0.76	0.37-1.57	82	103	0.60	0.33-1.09	0.60	0.33-1.09

* Conditional logistic regression models matched for age-group and health planning district, and adjusted additionally for age.

† Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

‡ Age when alcohol consumption stopped was missing for 1 case and 1 control.

§ Does not reflect actual duration of drinking; based on reported age at cessation or reference age minus first age of alcohol use.

TABLE 14. Odds ratios (OR) and 95% confidence intervals (CI) for age-adjusted models, and multivariate-adjusted full models for breast cancer risk associated with past alcohol intake at previous ages 25, 35, and 50, and average lifetime alcohol intake based on ages 25 through 50, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

Alcohol Exposure Variable	Hispanic						non-Hispanic White					
	Cases	Controls	Age-adjusted *		Full †		Cases	Controls	Age-adjusted *		Full †	
	No.	No.	OR	95%CI	OR	95%CI	No.	No.	OR	95%CI	OR	95%CI
Age 25, alcohol intake (grams/week) †‡§												
Nondrinker	83	82	1.00		1.00		51	46	1.00		1.00	
< 8	107	130	0.81	0.53-.124	1.11	0.67-1.86	112	126	0.85	0.52-1.40	0.86	0.50-1.50
8 - <21 (1 drink)	28	33	0.79	0.43-1.45	0.86	0.42-1.73	45	48	0.84	0.47-1.52	0.70	0.36-1.37
21 - <42 (2 drinks)	17	23	0.78	0.38-1.61	0.97	0.42-2.26	32	37	0.85	0.45-1.63	0.70	0.34-1.44
42 - <85 (3-4 drinks)	18	20	0.89	0.42-1.87	1.12	0.48-2.64	38	58	0.63	0.35-1.14	0.58	0.30-1.12
85 - <148 (5-7 drinks)	16	23	0.63	0.30-1.30	0.68	0.28-1.66	25	32	0.83	0.42-1.64	0.73	0.34-1.58
>= 148 (8+ drinks)							16	33	0.48	0.23-1.02	0.41	0.18-0.96
Drank at other times	63	77	0.77	0.48-1.23	0.84	0.48-1.46	61	76	0.71	0.41-1.22	0.66	0.36-1.20
Age 35, alcohol intake (grams/week) †‡§¶												
Nondrinker	83	79	1.00		1.00		50	45	1.00		1.00	
< 8	101	113	0.82	0.53-1.27	1.12	0.66-1.89	102	116	0.79	0.48-1.31	0.77	0.44-1.36
8 - <21 (1 drink)	28	36	0.67	0.36-1.22	0.80	0.39-1.64	45	50	0.80	0.44-1.45	0.68	0.34-1.34
21 - <42 (2 drinks)	17	27	0.67	0.33-1.36	0.74	0.33-1.63	29	37	0.76	0.40-1.47	0.64	0.31-1.34
42 - <85 (3-4 drinks)	27	18	1.32	0.66-2.64	2.10	0.89-4.92	35	64	0.48	0.26-0.88	0.47	0.24-0.93
85 - <148 (5-7 drinks)	15	24	0.53	0.25-1.11	0.54	0.22-1.32	32	18	1.62	0.78-3.34	1.54	0.69-3.41
>= 148 (8+ drinks)							27	30	0.82	0.41-1.62	0.88	0.40-1.93
Drank at other times	46	64	0.64	0.39-1.07	0.78	0.43-1.41	51	66	0.70	0.40-1.23	0.67	0.36-1.26
Unexposed, reference age <35	15	27					9	30				

Table 14. (Continued)

Alcohol Exposure Variable	Hispanic						non-Hispanic White					
	Cases	Controls	Age-adjusted *		Full †		Cases	Controls	Age-adjusted *		Full †	
	No.	No.	OR	95%CI	OR	95%CI	No.	No.	OR	95%CI	OR	95%CI
Age 50, alcohol intake (grams/week) †‡§¶												
Nondrinker	59	60	1.00		1.00		44	33	1.00		1.00	
< 8	51	47	1.11	0.62-1.98	1.08	0.52-2.26	59	50	0.80	0.44-1.48	0.88	0.44-1.74
8 - <21 (1 drink)	16	26	0.51	0.24-1.10	0.40	0.15-1.05	23	33	0.49	0.24-1.01	0.45	0.20-1.04
21 - <42 (2 drinks)	9	14	0.68	0.26-1.75	0.69	0.23-2.04	21	16	0.89	0.40-2.00	0.96	0.38-2.40
42 - <85 (3-4 drinks)	7	10	0.61	0.21-1.76	0.57	0.17-1.91	22	37	0.40	0.20-0.81	0.37	0.16-0.85
85 - <148 (5-7 drinks)	10	5	2.16	0.66-7.03	2.07	0.50-8.61	22	15	1.04	0.46-2.35	1.08	0.42-2.77
>= 148 (8+ drinks)							23	20	0.82	0.38-1.76	1.14	0.46-2.80
Drank at other times	33	47	0.68	0.37-1.27	0.61	0.29-1.31	47	36	0.87	0.45-1.68	1.01	0.48-2.11
Unexposed, reference age <50	147	179					119	216				
Average lifetime intake, ages 25 to 50 (grams/week) †‡§												
Nondrinker	83	82	1.00		1.00		51	46	1.00		1.00	
< 8	131	157	0.81	0.54-1.22	1.08	0.66-1.76	116	132	0.85	0.52-1.40	0.86	0.50-1.48
8 - <21 (1 drink)	31	37	0.77	0.43-1.39	0.90	0.46-1.78	50	63	0.72	0.41-1.26	0.56	0.29-1.07
21 - <42 (2 drinks)	32	40	0.84	0.47-1.50	0.96	0.49-1.88	36	58	0.60	0.33-1.09	0.53	0.27-1.04
42 - <85 (3-4 drinks)	19	23	0.77	0.38-1.56	1.23	0.53-2.81	57	70	0.78	0.45-1.36	0.70	0.38-1.32
85 - <148 (5-7 drinks)	23	28	0.73	0.38-1.40	0.67	0.30-1.48	32	29	1.00	0.51-1.95	0.76	0.36-1.60
>= 148 (8+ drinks)							27	39	0.65	0.34-1.26	0.70	0.33-1.47
Drank at other times	13	21	0.60	0.27-1.29	0.59	0.25-1.41	11	19	0.63	0.26-1.50	0.64	0.25-1.64

Table 14. (Continued)

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Alcohol intake in grams categorized as in analyses of 'recent' alcohol intake.

‡ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

§ The categories, former drinkers, drank at later ages, and current drinkers, but no data reported, were combined into 'drank at other times' because of small sample size and minimal change in estimates.

¶ Number of subjects at ages 35 and 50 based on total number of women whose reference age was equal to or greater than the age at alcohol intake (age 35 or age 50).

TABLE 15. Selected characteristics of cases, stratified by status of alcohol consumption at diagnosis (n=712), New Mexico Women's Health Study, 1992-1994

	Cases			
	Non-Drinkers	Current Drinkers	Former Drinkers	
			Stop 1+ years prior to diagnosis age	Stop within year of diagnosis age
Characteristic	(n=134)	(n=399)	(n=135)	(n=44)
Ethnicity				
Hispanic (%)	62	42	46	48
Non-Hispanic White (%)	38	58	54	52
Education, >12 years (%)	25	59	43	52
Age *[1]	58±11	52±11	55±11	48±10
Energy intake, kilocalories/day	2287±1003	2303±912	2171±856	2330±961
Total fat intake, grams/day †	87±44	89±42	83±41	95±50
Body mass index (kg/m^2)	26±5	23±4	25±6	24±4
Cigarette smoking (%)	26	53	49	39
History of fibrocystic disease(%)	14	22	20	18
Oral contraceptive use (%)*[2]	43	66	47	73
Breast cancer in mother, sister, daughter (%)	17	15	11	9
Vigorous physical activity, >35 METS (%)	16	17	14	20
Premenopausal status (%)*[3]	17	40	30	57
Stage, regional or remote (%)*[4]	35	27	30	58
Age at first use of alcohol		21±8	22±7	20±5
Duration of drinking (years) *[5]		31±11	21±12	28±10
Age 25, alcohol intake (drinks/week)		2.7±4.8 (330) ‡	2.5±5.8 (88)	2.0±2.6 (36)
Age 35, alcohol intake (drinks/week) §		3.4±6.2 (343)	2.9±5.5 (78)	2.3±2.4 (37)
Age 50, alcohol intake (drinks/week) §		3.9±6.5 (219)	4.1±8.03 (32)	2.9±2.6 (13)
Lifetime average intake (drinks/week)		3.1±5.2 (391)	2.5±5.0 (119)	2.1±2.4 (44)

Table 15. (Continued)

* Comparison of the two former drinker groups, $p<0.01$:
1 $F = 14.4$, $p=0.0002$
2 $\chi^2 = 9.0$, $p=0.003$
3 $\chi^2 = 16.5$, $p=0.000$
4 $\chi^2 = 10.8$, $p=0.001$
5 $F = 14.2$, $p=0.0002$

† Absolute intake.

‡ Number shown in parentheses equal to number of women who reported drinking at specific ages (25, 35, 50). The lifetime average intake does not always equal the total for each group, because 11 women reported alcohol intake between the age intervals for which data was collected, and 13 women stopped drinking before the age of 25.

§ Numbers of subjects at age 35 and 50, based on total number of women whose reference age was equal to or greater than the age at alcohol intake (age 35 or age 50).

TABLE 16. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with past alcohol intake stratified by ethnicity, excluding former drinkers who stopped within year of reference age, New Mexico Women's Health Study, 1992-1994 *

Alcohol Exposure Variable	Hispanic				non-Hispanic White			
	Cases	Controls			Cases	Controls		
	No.	No.	OR	95%CI	No.	No.	OR	95%CI
History of alcohol consumption								
Never	83	82	1.00		51	46	1.00	
Ever	228	304	0.89	0.57-1.41	306	407	0.69	0.41-1.14
Status of alcohol consumption at interview								
Nondrinker	83	82	1.00		51	46	1.00	
Current drinker	166	230	0.87	0.54-1.41	233	328	0.63	0.37-1.07
Former drinker	62	74	0.94	0.54-1.64	73	79	0.86	0.48-1.56
Age (years) at first alcohol use †								
Nondrinker	83	82	1.00		51	46	1.00	
<= 16	37	62	0.66	0.34-1.30	65	120	0.55	0.29-1.02
17 - 18	43	70	0.61	0.33-1.15	89	116	0.65	0.36-1.18
19 - 21	66	87	0.90	0.51-1.57	86	100	0.77	0.43-1.37
>= 22	82	85	1.12	0.66-1.90	66	71	0.70	0.39-1.28
Duration (years) of drinking ††								
Nondrinker	83	82	1.00		51	46	1.00	
< 10	21	32	0.84	0.40-1.75	16	21	0.71	0.30-1.71
10 - 39	181	223	0.96	0.59-1.57	213	285	0.77	0.45-1.32
>= 40	25	48	0.75	0.36-1.55	77	101	0.56	0.30-1.02
Age 25, alcohol intake (grams/week) §¶**								
Nondrinker	83	82	1.00		51	46	1.00	
< 8	97	130	1.01	0.60-1.71	105	125	0.84	0.48-1.47
8 - <21 (1 drink)	25	32	0.79	0.38-1.65	44	47	0.72	0.36-1.42
21 - <42 (2 drinks)	15	22	0.89	0.37-2.15	27	37	0.58	0.28-1.22
42 - <85 (3-4 drinks)	17	20	1.11	0.47-2.64	34	57	0.54	0.28-1.07
85 - <148 (5-7 drinks)	15	23	0.68	0.27-1.67	24	32	0.74	0.34-1.63
>= 148 (8+ drinks)					15	33	0.41	0.18-0.98
Drank at other times	59	77	0.81	0.46-1.41	57	76	0.62	0.34-1.14

Table 16. (Continued)

Alcohol Exposure Variable	Hispanic Cases No.	Hispanic Controls No.	Hispanic OR	Hispanic 95%CI	non-Hispanic White Cases No.	non-Hispanic White Controls No.	non-Hispanic White OR	non-Hispanic White 95%CI
Age 35, alcohol intake (grams/week) §¶#**								
Nondrinker	83	79	1.00		50	45	1.00	
< 8	92	113	1.06	0.62-1.82	96	115	0.76	0.43-1.34
8 - <21 (1 drink)	25	36	0.74	0.35-1.55	44	49	0.70	0.35-1.39
21 - <42 (2 drinks)	14	26	0.63	0.27-1.46	27	37	0.59	0.28-1.26
42 - <85 (3-4 drinks)	24	18	1.79	0.74-4.31	30	63	0.41	0.20-0.83
85 - <148 (5-7 drinks)	14	24	0.52	0.21-1.29	28	18	1.36	0.60-3.06
>= 148 (8+ drinks)					27	30	0.91	0.42-2.01
Drank at other times	45	64	0.76	0.42-1.38	47	66	0.61	0.32-1.16
Unexposed, reference age <35	15	27			9	30		
Age 50, alcohol intake (grams/week) §¶#**								
Nondrinker	59	60	1.00		44	33	1.00	
< 8	48	47	1.01	0.48-2.13	58	50	0.87	0.44-1.73
8 - <21 (1 drink)	16	26	0.41	0.16-1.08	22	32	0.42	0.18-0.98
21 - <42 (2 drinks)	8	13	0.63	0.20-1.99	20	15	0.96	0.37-2.45
42 - <85 (3-4 drinks)	7	10	0.57	0.17-1.89	19	36	0.30	0.13-0.72
85 - <148 (5-7 drinks)	10	5	2.03	0.48-8.54	19	15	0.90	0.34-2.39
>= 148 (8+ drinks)					23	20	1.16	0.47-2.87
Drank at other times	30	47	0.60	0.27-1.27	45	36	0.94	0.45-1.97
Unexposed, reference age <50	147	179			250	237		
Average lifetime intake, ages 25 to 50 (grams/week) §¶**								
Nondrinker	83	82	1.00		51	46	1.00	
< 8	120	157	1.01	0.61-1.66	109	132	0.83	0.48-1.45
8 - <21 (1 drink)	29	36	0.88	0.44-1.77	48	61	0.57	0.29-1.09
21 - <42 (2 drinks)	27	39	0.78	0.39-1.57	30	58	0.43	0.21-0.86
42 - <85 (3-4 drinks)	18	23	1.20	0.52-2.79	51	69	0.65	0.34-1.23
85 - <148 (5-7 drinks)	21	28	0.65	0.29-1.45	30	29	0.73	0.34-1.57
>= 148 (8+ drinks)					27	39	0.72	0.34-1.52
Drank at other times	13	21	0.61	0.25-1.45	11	19	0.66	0.25-1.69

Table 16. (Continued)

Alcohol Exposure Variable	Hispanic				non-Hispanic White			
	Cases	Controls			Cases	Controls		
	No.	No.	OR	95%CI	No.	No.	OR	95%CI
Recent alcohol intake (grams/week) §¶‡‡								
Nondrinker §§	200	235	1.00		179	187	1.00	
< 8	32	43	1.31	0.73-2.33	29	46	0.48	0.27-0.86
8 - <21 (1 drink)	25	38	0.95	0.50-1.79	31	57	0.46	0.26-0.80
21 - <42 (2 drinks)	20	29	0.67	0.32-1.40	29	54	0.47	0.25-0.80
42 - <85 (3-4 drinks)	12	15	1.22	0.50-2.96	34	49	0.60	0.34-1.06
85 - <148 (5-7 drinks)	17	17	1.48	0.67-3.27	16	28	0.48	0.23-1.00
>= 148 (8+ drinks)	0	0			36	27	1.60	0.87-2.97

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Age when alcohol consumption stopped was missing for 1 case and 1 control.

‡ Does not reflect actual duration of drinking; based on reported age at cessation or reference age minus first age of alcohol use.

§ Absolute intake.

¶ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

Number of subjects at ages 35 and 50 based on total number of women whose reference age was equal to or greater than the age at alcohol intake (age 35 or age 50).

** The categories, former drinkers, drank at later ages, and current drinkers, but no data reported, were combined into 'drank at other times' because of small sample size and minimal change in estimates.

‡‡ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.

§§ No intake in four-week period, six months in past.

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APPENDIX I

"Alcohol Consumption and Breast Cancer Risk Among
Hispanic and non-Hispanic White Women in New Mexico"
(Doctoral Dissertation)

(The pagination of Appendix I for this report is in the lower right-hand corner of the page.
The centered page numbers refer to the original page numbering of the dissertation.)

ALCOHOL CONSUMPTION AND BREAST CANCER RISK AMONG HISPANIC AND NON-HISPANIC WHITE WOMEN IN NEW MEXICO

By

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DISSERTATION

Presented to the Faculty of The University of Texas-

Houston Health Science Center

School of Public Health

in Partial Fulfillment

of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

THE UNIVERSITY OF TEXAS-HOUSTON HEALTH SCIENCE CENTER
SCHOOL OF PUBLIC HEALTH
Houston, Texas
May, 1999

PREFACE

This work was supported by a grant award through the United States Army Medical Research and Materiel Command, Department of Defense Breast Cancer Research Program (DAMD17-96-1-6227). A manuscript has been developed from this thesis and will be submitted for consideration for publication to the *American Journal of Epidemiology*.

ACKNOWLEDGMENTS

I gratefully acknowledge the support and guidance provided by my committee members at the University of Texas School of Public Health, Drs. Fred Annegers, Ralph Frankowski, and Susie McPherson. Additionally, I appreciate the guidance I received from Dr. Jonathan Samet, Department of Epidemiology, Johns Hopkins University, the original Principal Investigator of the 'New Mexico Women's Health Study'. Appreciation is extended to Dr. Frank Gilliland, School of Medicine, University of Southern California who also served as the Principal Investigator for this study, to Dr. Charles Key, Director of the New Mexico Tumor Registry, and to Dr. David Coultas, Director of Epidemiology and Cancer Control, University of New Mexico School of Medicine.

Dissertation submitted to the Ph.D. Committee on April 1, 1999.

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ABSTRACT

Many studies have shown a consistent increased breast cancer risk associated with modest or high alcohol intake, but few included Hispanic women. The alcohol-breast cancer association was investigated in a New Mexico statewide population-based case-control study. The New Mexico Tumor Registry ascertained cases (n=712), newly diagnosed with breast cancer (1992-1994) aged 30-74 years. Controls (n=844) were identified by random digit dialing and frequency-matched for ethnicity, age-group, and health planning district. In-person interviews were conducted, and data collected for breast cancer risk factors, including recent and past alcohol intake. Results for past alcohol intake and a breast cancer association did not show any trend and were nonsignificant. Multivariate-adjusted odds ratios for recent alcohol intake and breast cancer suggested an increased risk at the highest level for both ethnic groups, but estimates were unstable and statistically nonsignificant. Low level of recent alcohol intake (<148 grams/week) was associated with a reduced risk for non-Hispanic whites (Odds Ratio (OR)=0.49 95% Confidence Interval (CI) 0.35-0.69). This pattern was independent of hormone-receptor status. The reduced breast cancer risk for low alcohol intake was present for premenopausal (OR=0.29, 95% CI 0.15-0.56) and postmenopausal women (OR=0.56, 95% CI 0.35-0.90).

Key Words: breast cancer; epidemiology, case-control study; alcohol; hormone-receptor status; Hispanics

Breast cancer is the most frequent cancer among Hispanic women (1). Although breast cancer incidence and mortality rates for Hispanic women are lower than those for non-Hispanic white women, they have increased more rapidly among Hispanic women (2-6). In New Mexico, breast cancer incidence rates for Hispanic women increased by 56 percent over the 19-year period 1969-1972, and mortality by 82 percent over the 30-year period 1958-1987 (2). The corresponding increases in non-Hispanic white women were 17 percent for incidence and 35 percent for mortality. Age-adjusted incidence rates for New Mexican Hispanic women increased from 57/100,000 to 74/100,000 for the time-periods 1983-1987 and 1988-1992, compared with 96/100,000 to 107/100,000 for non-Hispanic white women (7).

There are few data available on breast cancer risk factors for Hispanic women (2, 3, 8-10). In particular, data are insufficient for dietary and alcohol practices (11). New Mexican Hispanic women, especially those over age 50, are reported to have lower alcohol intake and more likely to be nondrinkers than non-Hispanic white women (12). In the one known study to evaluate alcohol consumption and breast cancer among Hispanics, an increased risk was suggested for postmenopausal women (Odds Ratio (OR)=1.24 for 13 grams(g)/day, 95 percent confidence interval (CI) 0.70-2.19), compared with non-Hispanic white women (OR=1.10 95 percent CI 0.99-1.22) (13).

Increased risk (30-70 percent) of breast cancer has been reported to be associated with modest to high alcohol intake among both premenopausal and postmenopausal women (14-16). 'Recent', 'past', and 'lifetime' alcohol consumption have been reported to increase risk

of breast cancer (13, 14, 16, 17). However, evidence suggests that recent intake may be most important, possibly acting as a late-stage promoter (14, 16, 18, 19).

Alcohol consumption has also been associated with specific hormone-receptor breast cancers (20, 21). Estrogen-receptor (ER) or progesterone-receptor (PR) status are important biological characteristics of breast tumors and are associated with response to endocrine therapy and better prognosis (22). Estrogen receptors are estrogen-binding proteins and are present in the nucleus of estrogen-responsive breast cells (23). These proteins regulate estrogen effect on growth and differentiation of normal breast epithelium (24). Women who have ER+PR+ breast cancer tumors have a better response to endocrine therapy and a better overall survival rate compared with women who have ER-PR- tumors (25-27). Elledge et al. (28) reported that Hispanic women were less likely to have ER+ or PR+ tumors than non-Hispanic white women, but another study reported no difference in joint ER/PR status by ethnicity (29). Hormone-receptor groups are also thought to be associated with different etiologic risk factors (23, 30-32).

The 'New Mexico Women's Health Study' (NMWHS), a statewide population-based case-control study, was initiated in 1992 to investigate etiologic risk factors for breast cancer among Hispanic and non-Hispanic white women. These data were used to investigate three hypotheses by menopausal status: alcohol consumption is associated with an increased breast cancer risk among Hispanic and non-Hispanic white women; this risk is higher in Hispanics than non-Hispanic whites; and, alcohol intake is associated with an increased risk for hormone-receptor negative breast cancer.

MATERIALS AND METHODS

Subject recruitment

Women newly diagnosed with an invasive or *in situ* breast carcinoma were eligible for inclusion in the NMWHS based on the following criteria: age 30-74 years, diagnosis between 1992-1994, and New Mexico residency at diagnosis. Cases were ascertained through the New Mexico Tumor Registry's (NMTR) rapid ascertainment system. The NMTR is one of the Surveillance, Epidemiology and End Results Programs (SEER) of the National Cancer Institute. New Mexico has the largest percentage of Hispanics (40 percent) to total state population in the US (33), accounting for the second largest (10 percent) sector of Hispanic SEER coverage (6).

All eligible Hispanic cases were included. The expected number of breast cancer cases for the study period was approximately three times higher for non-Hispanic whites compared with Hispanics. A 33 percent random sample of non-Hispanic white cases based on age-group (30-39, 40-64, 65-74 years), and geographic region (seven state health planning districts), was identified for inclusion. The sampling fraction for non-Hispanic white cases was chosen to give a distribution similar to the age and geographic distribution of Hispanic cases ascertained by the NMTR during the period 1988-1990. A total of 491 eligible Hispanic breast cancer cases was ascertained. Random selection of non-Hispanic whites resulted in 493 cases. Of the eligible cases, 332 Hispanic (68 percent) and 380 non-Hispanic white women (77 percent) completed interviews.

Controls were frequency-matched on the basis of Hispanic and non-Hispanic white ethnicity, age-group, and health planning district. Women were recruited by using a modified

approach to the Waksberg random digit dialing method (34). Data from the NMTR collected over the previous 26 years were used to build a prefix pool known to contain residential numbers for control selection. This restricted pool was based on prefixes which had contributed at least one breast cancer case to the NMTR database. It was used to increase the likelihood of generating a larger number of 'working' residential phone numbers; a real concern due to New Mexico's sparse population. Additionally, a random sample of phone numbers linked to gender, ethnicity, age-group, and health planning district were used to efficiently locate and recruit a sufficient number of older, rural Hispanic controls due to the difficulty in ascertaining this subset of women.

A total of 8,147 working telephone numbers were contacted; of these, 4,459 were residential numbers. There were a total of 1,039 eligible controls ascertained from 3,400 respondents who completed the telephone screening interview; 511 Hispanic and 528 non-Hispanic white women. Of these, 388 (76 percent) Hispanic and 456 (86 percent) non-Hispanic white women completed interviews. Reasons for subject nonparticipation are provided in greater detail elsewhere (35).

Data collection

The NMWHS project was approved by the University of New Mexico's Human Research Review Committee. Physician consent was obtained for all cases, and participants signed a written informed consent prior to the interview. All questionnaires were translated into Spanish, and interviews were conducted in Spanish or English according to the participant's preference. Interviews were conducted in-person at a subject's home or an agreed upon location, and averaged 1½ hours.

Recent dietary and alcohol intake was collected at the beginning of the interview, using a modified version of a quantitative food frequency questionnaire (FFQ) designed by the staff of the Human Nutrition Center at the University of Texas-Houston, School of Public Health. This FFQ was previously used in a Texas Hispanic population (36). Modifications, based on an analysis of food intake recalls of 100 women, were made by Dr. RS McPherson to add foods to the FFQ that were important sources of nutrients among New Mexico women. The final FFQ instrument was developed using standard protocols and included 140 items (37, 38). Frequency of use information included consumption on a per month (28 day), week, or day basis and portion size consumed. Two-dimensional food models were used to aid in the determination of amount consumed. Frequency of consumption and portion size data were entered into the 'Food Frequency Data Entry and Analysis Program' containing the gram weight and nutrient data to calculate nutrient estimates per food per day, and total nutrient intake per day (39, 40). In an effort to avoid the potential impact of disease or treatment on diet, all subjects were asked to recall 'usual' food intake for a four-week period, six months prior to the interview.

'Recent' alcohol intake, as measured by the FFQ, was expressed as the average daily consumption of the summation of wine, beer, and hard-liquor intake. This was converted to a weekly intake for analysis. The ethanol content for each type of beverage was based on the amount reported in the US Department of Agriculture (USDA) Nutrient Database for Individual Intake Surveys: 8.132 g/alcohol for one 3 ½-ounce glass of wine; 12.6 g/alcohol for one serving of beer; and 21.2 g/alcohol for one hard-liquor drink (40). Alcohol abstinence (nondrinkers) was defined as an intake of 0 g/day.

A 'Risk Factor Questionnaire' (RFQ) was used to collect data on demographic characteristics and breast cancer risk factors. A calendar was used to record major life events as an assistance to recall. Data on breast cancer risk factors were collected for reproductive and menstrual history, use of oral contraceptives and exogenous hormones, family history and personal history of breast disease, weight, height, physical activity during the prior year, history of cigarette smoking, and alcohol consumption. The questions on alcohol intake included ever *vs.* never use, age at first use, age at cessation, frequency of drinking, and number of weekly drinks by beverage type at age 25, 35 and 50 years. Frequency of drinking included daily, weekly, monthly and yearly categories. The number of drinks per week for subjects reporting consumption on a monthly or yearly basis was estimated based on the frequency midpoint divided by the number of weeks per time interval. The ethanol content in grams was multiplied by the number of weekly drinks per beverage type to estimate gram intake/week.

Hormone-receptor assays were conducted in laboratories associated with the hospitals where cases were diagnosed. Estrogen and progesterone receptor status was recorded by NMTR abstractors. The criteria used to classify menopausal status have been described elsewhere in a previous analysis of reproductive factors (35). Final categories included premenopausal, postmenopausal, and surgical unknown. Body mass index (BMI) was calculated as weight in kilograms(kg)/height in meters squared(m^2). Metabolic equivalents (METS) were calculated for physical activity as kilocalories (kcals)/kg of weight/hour (41). The assigned metabolic equivalents were multiplied by the mean number of hours/week to compute final METS.

Statistical analysis

Multivariate logistic regression was used to determine age-adjusted and multivariate odds ratios and corresponding 95 percent confidence intervals for alcohol exposure variables adjusting for covariates (42). Ethnic-specific logistic regression analyses were conditioned on the matching factors age-group and health planning district. Polytomous logistic regression analysis was used to estimate odds ratios for the joint classification of hormone-receptor status, when both receptors were known, relative to controls. Joint categories included (ER+PR+, ER-PR-, ER+PR-, ER-PR+) (42). Logistic regression analyses were computed using STATA software (43).

The alcohol exposure variables investigated included recent intake collected on the FFQ, and history of alcohol consumption defined as ever *vs.* never use, status of alcohol consumption at time of interview (nondrinker, current drinker, former drinker), age at first use, years since last consumption, years of drinking, gram intake/week at ages 25, 35, and 50, and average lifetime intake based on data for the latter three ages, as collected on the RFQ. Specific beverage type was not analyzed, because there has not been consistent evidence to suggest an effect independent of ethanol content (15, 17, 19, 44). Additionally, it is difficult to estimate the separate effects due to each beverage type, since women tend to drink a combination of alcoholic beverages (14).

Covariates in previous studies of alcohol consumption and breast cancer risk were included as potential confounders (13, 14, 16, 17, 23, 44-50). These included education, age at menarche, age at first full-term birth (FFTB) for pregnancies lasting six months or longer regardless of pregnancy outcome, number of full-term births lasting six months or longer

(single birth, multiple birth, stillbirth), cumulative months of lactation for all children, cumulative years of oral contraceptive use, menopausal status, history of fibrocystic disease, breast cancer in mother, sister, or daughter, history of cigarette smoking lasting for more than six months, usual adult BMI, physical activity, energy intake, and energy-adjusted total fat intake. Logistic regression models included all covariates to allow comparison of results between ethnic and menopausal status groups. Analyses were also stratified by ethnicity and menopausal status to evaluate whether different sets of confounders were important across strata. The change-in-estimate method was used to identify the most important confounders within each ethnic and menopausal specific model by comparing models containing all covariates with models excluding each covariate (51). Interaction between menopausal status and alcohol was investigated by comparing models, with and without product terms, using the log likelihood test statistic (42). Menopausal status may be a marker for change in endogenous hormones, and therefore a critical effect-modifier of the alcohol-breast cancer association (13). It was included in all models, because it has been shown to be important in previous analyses of reproductive variables for the NMWHS (35).

Age, defined as age at diagnosis for cases and age at interview for controls, was included in all models to adjust for residual age differences between cases and controls. Category boundaries for covariates that were not dichotomous were defined either on the basis of commonly accepted cutpoints, or on the basis of the distribution among controls. Alcohol-related variables were categorized by the number of grams/week. Categorical variables were evaluated to determine whether final groupings were too few to detect dose-response changes or too many to provide stable estimates (51). Total fat intake was highly

correlated with energy intake (Spearman's rank correlation coefficient, r=0.91), and was energy-adjusted based on the residual method (52). Alcohol use was not energy-adjusted as it was weakly correlated with total energy intake (r=0.15), as shown in other studies (52).

Subjects with an energy intake outside the range of 500-6,000 kcals were excluded. Exclusions were due to 16 subjects with an energy intake >6,000 kcals/day, and all but one had a low alcohol intake <10 g/day. Seven subjects were excluded due to incomplete or no FFQ data. Additional deletions were related to missing data for covariates included in the models.

RESULTS

Descriptive analyses

The majority of cases were diagnosed with intraductal carcinoma (66 percent), followed by lobular carcinoma (9 percent). Although distributions for stage at diagnosis followed the same trend for both ethnic groups, with local disease accounting for 52 percent of cases, regional disease at diagnosis was higher for Hispanics (33 percent) compared with non-Hispanic whites (25 percent). Co-morbid conditions were similar in distribution by both case-control status and ethnicity with the exception of diabetes, gallbladder disease, and rheumatoid arthritis, which were higher in Hispanic women, at 12, 19, and 11 percent, compared with non-Hispanic white women at 4, 13, and 6 percent, respectively.

The mean age of cases at diagnosis was 54 years compared with 53 years for controls at time of interview. Distribution of selected characteristics for cases and controls have been previously reported (35). Hispanic women, compared with non-Hispanic white women, were generally younger at their FFTB, had a higher parity, higher BMI (>=25 kg/m^2), and less

education (35). They did not report a history of fibrocystic disease or a family history of breast cancer as frequently as non-Hispanic whites (35). Hispanics (36 percent) reported a low level of physical activity more frequently than non-Hispanic whites (24 percent). In general, Hispanic women, compared with non-Hispanic white women, reported higher median levels of daily total energy intake (2,257 *vs.* 2,107 kcals/day) and total fat intake (85 *vs.* 80 g/day).

Hispanic women reported a history of past alcohol consumption less frequently than non-Hispanic white women (77 *vs.* 88 percent), and cases were similar to controls (81 *vs.* 85 percent). Of these women, 42 percent of cases and 48 percent of controls reported recent alcohol intake during the one month period, six months prior to interview. Reported recent alcohol intake was low with 55 percent of Hispanics and 38 percent of non-Hispanic whites reporting an intake of less than one drink/week.

Age-adjusted covariates

Age-adjusted odds ratios for breast cancer risk factors are shown in table 1. Patterns differed by ethnicity. A high BMI was the strongest statistically significant risk factor (OR=2.38 for >=25 kg/m^2) and vigorous physical activity was the strongest protective factor (OR=0.34 for >=35 METS)/week) among Hispanic women. Among non-Hispanic whites, a positive history of fibrocystic disease (OR=1.68) was the strongest risk factor, whereas 12 months or more of lactation (OR=0.53), and vigorous physical activity (OR=0.55 for >=35 METS/week) were strong protective factors. High intake of energy and total fat appeared to be protective in non-Hispanic whites, but not in Hispanics. All covariates listed in table 1

were kept in the final models, so comparisons could be made across ethnic and menopausal status groups. The effects of specific covariates are described below.

Recent alcohol intake

Data from a previous pilot study were used to assess the validity and reproducibility of alcohol intake as measured by the FFQ. These data were based on 132 volunteer New Mexico Hispanic and non-Hispanic white women, aged 35 to 74 years, with and without a breast cancer history (53). The Spearman correlation coefficient between alcohol intake during the past month and intake for the same month, recalled six months later, was 0.83. Results were comparable for cases (r=0.82) and noncases (r=0.85), but were lower for Hispanics (r=0.73) compared with non-Hispanic whites (r=0.87). This reproducibility for alcohol intake is comparable to that reported in previous studies (45, 54, 55).

The age-adjusted odds ratio for recent alcohol intake was 1.42 (95 percent CI 0.82-2.46) for non-Hispanic white women consuming >=148 g/week (8+ drinks/week), and 1.14 (95 percent CI 0.56-2.29) for Hispanic women consuming >=85 g/week (5+ drinks/week) as compared to nondrinkers (table 2). Multivariate adjustment increased these odds ratios to 1.56 (95 percent CI 0.85-2.86) and 1.35 (95 percent CI 0.63-2.93), respectively (table 2). Low level of recent alcohol intake (<8 drinks/week) was associated with a consistent reduced risk of approximately 50 percent in the multivariate full model for non-Hispanic white women (table 2). Overall, there was no evidence of an alcohol effect on breast cancer risk in Hispanic women.

Analyses based on reduced models including the strongest ethnic-menopausal confounders (>=20 percent change in the odds ratio, table A_1, see Appendix A for tables

with an 'A' prefix), did not produce estimates that were substantially different from the full models containing all covariates or the age-adjusted models. In a reduced model for Hispanic women (table A_2), in which fibrocystic disease and smoking were excluded, point estimates differed from those in the corresponding full model (table 2) by less than 11 percent. In non-Hispanic white women, a reduced model including only BMI, energy intake, and smoking produced an odds ratio of 1.65 (95 percent CI 0.93-2.92) for the highest level of alcohol intake (>148 g/week), and odds ratios ranging from 0.49 to 0.72 for alcohol intake levels less than 148 g/week (table A_2). Further elimination of cigarette smoking from the reduced model for non-Hispanic whites produced the same results for all intake levels, with the exception of the highest level which was reduced to the same estimate as shown for the full model (OR=1.56) (data not shown). Table A_3 shows results for the same analyses stratified by menopausal status. On average, across ethnic and menopausal groups, the estimates based on the reduced models did not differ by more than 15 percent from the full models, and did not always enhance the magnitude of the effects. In general, no strong confounders of alcohol intake and breast cancer emerged in the analyses. The comparison of full *vs.* reduced *vs.* age-adjusted models did not suggest any problems with overfitting due to the inclusion of all covariates in the full models (42).

Recent alcohol intake was further collapsed into fewer categories, based on lack of trend. These included four categories (nondrinker, <8, 8-<42, >=42 grams/week) for Hispanics, and three categories (nondrinker, <148, >=148 grams/week) for non-Hispanic whites. Among non-Hispanic white women, there was a statistically significant reduced risk for breast cancer (OR=0.49, 95 percent CI 0.35-0.69) among women reporting fewer than 8

drinks/week compared to nondrinkers. This reduced risk for low alcohol intake was also present for premenopausal (OR=0.29, 95 percent CI 0.15-0.56) and postmenopausal non-Hispanic white women (OR=0.56, 95 percent CI 0.35-0.90) (table 3). There was no consistent evidence for a protective effect of low to moderate alcohol intake in Hispanics by menopausal status. There was a suggestion of an increased risk at the highest level among postmenopausal women for both ethnic groups, but estimates were unstable and statistically nonsignificant (table 3).

Hormone-receptor status and recent alcohol intake

The distribution for ethnic-specific hormone-receptor status was similar with the exception of ER-/PR- (24 percent for Hispanic *vs.* 17 percent for non-Hispanic white). About 40 percent in each ethnic group were ER+/PR+; 10 to 12 percent were ER+/PR-; 3 percent were ER-/PR+; and 9 to 12 percent were unknown. In the polytomous logistic regression analysis of recent alcohol intake, only ER+/PR+ and ER-/PR- were included, and each case group compared simultaneously with the controls. Stratification was limited to ethnicity as stratum-specific numbers were too small to additionally stratify by menopausal status. The direction of the odds ratios was similar for the two hormone-receptor status groups (table 4). Odds ratios for ER+/PR+ status were statistically significant for both low (OR=0.46, 95 percent CI 0.28-0.74), and high alcohol intake (OR=2.13, 95 percent CI 1.03-4.43) (table 4). An increased risk for non-Hispanic whites associated with an intake of 8+ drinks/week was 50 percent higher for ER+PR+ compared with ER-PR- status, but the difference was not statistically significant.

Past alcohol intake

Results for ever *vs.* never alcohol consumption did not show a significant association with breast cancer in the age-adjusted analysis for Hispanic women (OR=0.78, 95 percent CI 0.54-1.14), or for non-Hispanic white women (OR=0.76, 95 percent CI 0.49-1.19) (data not shown). Multivariate adjustment did not alter these results (table 5). Multivariate analyses were performed to test for interaction between menopausal status and ever *vs.* never alcohol intake. The associated risk for Hispanic women was increased, but was not statistically significant (OR=1.50 95 percent CI 0.63-3.57; -2 log likelihood test statistic: χ^2= 1.56, p=0.21).

Risk of breast cancer did not vary by age at first use or by duration of drinking (table 5). There was no suggestion of an alcohol effect for lifetime average intake or for ages 25, 35, and 50 (table A_4). Overall, most risk estimates were less than 1.0, and none were statistically significant. A minimal risk for Hispanic and non-Hispanic white former drinkers was present, but this was due primarily to the 44 cases who reported cessation of drinking within year of diagnosis (OR=12.13 for Hispanic; OR=8.04 for non-Hispanic white, table 5). Risk decreased as years since last alcohol consumption increased (table 5). These cases had more severe disease (regional/remote) at diagnosis (58 *vs.* 42 percent), were younger (48 *vs.* 54 years) than other cases, and reported the lowest level of average lifetime alcohol intake (32 *vs.* 48 g/week) (data not shown). (Table A_5 provides a comparison of selected characteristics for these women compared to other cases.) Exclusion of this group produced estimates close to 1.0 for former drinkers among Hispanics (OR=0.94) and non-Hispanic

whites (OR=0.86) (data not shown). All other analyses of past and recent alcohol intake were no more than 10 percent different when these subjects were excluded (data not shown).

DISCUSSION

A consistent finding in this study was a protective effect for light to moderate alcohol intake (<8 drinks/week) in non-Hispanic white women. However, results were only statistically significant for recent intake. There was a suggestion of an increased risk for breast cancer among postmenopausal Hispanic and non-Hispanic white women at the highest alcohol intake level, and that menopausal status may be an effect-modifier in Hispanic women. The latter finding has been suggested in previous studies (16, 48, 56-58), but results have not always been consistent. Results for age at first use of alcohol and duration of drinking did not show a risk for breast cancer, but these have not been consistent risk factors (50, 59-61). The pattern of a protective effect at low alcohol intake, and a suggested risk at higher intake in non-Hispanic white women was seen regardless of hormone-receptor status. Investigations of hormone-receptor status and breast cancer risk factors have not shown a consistent association for other risk factors (reproductive-related, smoking, BMI, diet) (23, 30-32, 62, 63). It is difficult to determine whether differences between hormone-receptor cancer type is associated with etiologic factors or to biological changes that occur during breast cancer development (29).

Generally, studies have demonstrated a consistent, but modest, increased risk with high alcohol intake, differing as to whether the effect is stronger for recent (14, 44, 45) or lifetime intake (13, 16). Results based on a recent analysis of the Framingham cohort did not show any evidence for an increased risk of breast cancer associated with long-term, light to

moderate alcohol consumption (64). The majority of studies have found evidence for a dose-response relationship (19), also supported in several meta-analyses (15, 44, 46). Longnecker et al.'s case-control study results (16), based on 15,825 subjects, showed a monotonic dose-response relationship for all women, but strongest for postmenopausal women. Swanson et al. (14) reported a threshold for increased risk at high levels of intake (≥14 drinks/week) for premenopausal women. The data from the present study suggest a weak association for a risk threshold, but at a lower level of intake than previously reported (14), and among only postmenopausal women. The suggestion of a greater alcohol-breast cancer association among postmenopausal Hispanic women, compared with non-Hispanic white women, as reported in Longnecker et al.'s study (13), was not replicated. Hispanic postmenopausal women were similar to non-Hispanic white women with about a two-fold increased risk, but at fewer drinks/week (3+ *vs.* 8+); however, these estimates were unstable and not statistically significant.

The present study was not able to evaluate heavy alcohol consumption, especially among Hispanics, because there were so few drinkers with a high intake. The relatively low level of alcohol consumption observed in this study has been reported previously in another New Mexico study (65). Studies in other regions of the US have also reported a lower average alcohol intake for Hispanics compared with non-Hispanics (3 *vs.* 5 drinks/week) (11, 66).

A lower response rate was observed in the present study for Hispanics compared with non-Hispanic whites. Response rates for cases were lower than for controls, and lower than that reported by Swanson et al. (86 percent) (14), but fell into the range reported by

Longnecker et al. across several states in a multi-centered study (74-86 percent) (16). Response rates for controls were comparable to that for previous studies (14, 16).

It is not possible to determine at this time whether the protective effect observed in non-Hispanic white women for low to moderate alcohol intake is indirect and due to confounding with other unadjusted health-related behaviors, due to an undetected information bias, or due to a direct biological effect inhibiting breast cancer induction or promotion. There was no single strong confounder of alcohol intake that explained the pattern in either ethnic group. This suggests that both the protective effect, as well as the possible threshold for increased risk, observed in non-Hispanic white women, is not due to the confounders included in analysis. Information bias could explain the reduced risk in non-Hispanic white cases if they systematically underreported their true alcohol intake. Previous studies of the effect of recall bias on reported alcohol consumption, however, have found little evidence for more than a modest effect when comparing retrospective to prospective assessment (67). There was evidence that a small group of women stopped drinking at the time of diagnosis, possibly due to information regarding an alcohol-breast cancer association. This may have led to recall bias by these women if they tended to underreport past or recent intake. However, removal of their data from analyses did not appear to meaningfully alter estimates. Although other studies have detected an increased risk for former drinkers compared with nondrinkers (56, 68), this may be primarily a reflection of time since cessation of alcohol intake.

Biological data suggest that high alcohol intake may increase breast cancer risk by one of several mechanisms: producing a direct mitogenic effect on breast tissues; increasing

serum concentrations of estrogens by either an effect on hepatic or pituitary-gonadal function; or, acting as a cocarcinogen (69-72). At present, most data support the hypothesis that alcohol increases circulating concentrations of estrogens. The association between alcohol and hormone levels is not straightforward. Several observational studies have reported that alcohol intake is associated with increased plasma or urinary estrogens in postmenopausal women (73-76). However, it has also been reported that acute alcohol ingestion increases blood estrogens only in postmenopausal women who are taking estrogen replacement therapy (70). Dorgan et al. (77) did not find an association between alcohol intake and plasma estrogens in premenopausal women across the menstrual cycle. Reichman et al. (69), however, reported that an alcohol dose of 30 g/day increased estrogen concentrations in a controlled, randomized trial in premenopausal women. Most investigations have been based on small, volunteer samples of women, and in such studies it is difficult to account for binge drinking, variability in alcohol metabolism, and alcohol-plasma hormone levels over several menstrual cycles (77).

A mechanism whereby a low alcohol intake might decrease risk is unknown at this time. The presence of this finding for both premenopausal and postmenopausal non-Hispanic white women seems to argue against an effect mediated by a change in hormone level. Whatever the explanation may be, whether real or spurious, the present study is not the only one to find a potential protective effect for light to moderate alcohol consumption. Longnecker et al.'s (13) study of alcohol consumption among postmenopausal women showed evidence for a modest protective effect associated with lifetime alcohol intake at low levels (OR=0.88 95 percent CI 0.67-1.15 for >0-5 g/day; OR=0.70 95 percent CI 0.51-0.94

for 6-11 g/day). Only a few other studies have reported a protective effect associated with a low alcohol level, and these have varied depending on menopausal status (60, 78, 79).

In conclusion, the results of the present study indicate that alcohol intake is not a risk factor for breast cancer in New Mexico Hispanic women. It does not seem likely that alcohol intake explains the increasing incidence of breast cancer in New Mexico Hispanic women, because there appears to be no consistent relationship in the low to moderate range observed, and high alcohol intake is rare. More research is needed to determine whether the reduced risk for low intake can be replicated in other studies, or is an artifact due to bias or unmeasured confounders in the present study.

(An Appendix providing a more detailed review of background studies was included in the dissertation, but has been excluded, because it is provided in the main report under 'BACKGROUND - PREVIOUS STUDIES', page 10.)

TABLE 1. Age-adjusted odds ratios (OR) and 95% confidence intervals (CI) for risk factors of breast cancer, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994 *

Risk Factor	Hispanic				non-Hispanic White			
	Cases (n=332) No. †	Controls (n=388) No.	OR	95%CI	Cases (n=380) No.	Controls (n=456) No.	OR	95%CI
Education (years)								
< 12	104	86	1.47	0.99-2.18	24	29	0.88	0.48-1.64
12	129	150	1.00		102	111	1.00	
> 12	96	152	0.68	0.47-0.97	253	315	0.89	0.64-1.25
Age (years) at menarche								
<= 12	133	170	0.88	0.60-1.28	185	211	1.15	0.80-1.64
13	101	109	1.08	0.72-1.61	111	140	1.03	0.70-1.53
>= 14	95	108	1.00		84	103	1.00	
Age (years) at first full-term birth								
<= 18	71	89	1.00		43	67	1.00	
19-20	71	94	1.02	0.65-1.59	60	73	1.19	0.71-2.01
21-22	50	64	1.04	0.64-1.71	59	64	1.32	0.77-2.45
23-26	62	68	1.14	0.70-1.84	82	95	1.33	0.81-2.18
>= 27	40	43	1.23	0.71-2.13	76	84	1.53	0.94-2.60
Nulliparous	38	30	1.54	0.85-2.77	60	73	1.30	0.77-2.22
Number of full-term births								
Nulliparous	38	30	1.46	0.83-2.57	60	73	1.33	0.81-2.19
1	29	35	0.99	0.55-1.79	63	58	1.90	1.13-3.17
2	66	98	0.78	0.51-1.20	128	138	1.56	1.02-2.40
3	80	72	1.43	0.93-2.18	66	101	0.94	0.59-1.50
>= 4	119	153	1.00		63	86	1.00	
Cumulative months of lactation								
Nulliparous	38	30	1.30	0.75-2.26	60	73	0.96	0.62-1.51
Parous, 1-12	109	128	0.93	0.65-1.34	167	157	1.24	0.88-1.76
Parous, >12	52	82	0.68	0.44-1.06	43	99	0.53	0.34-0.84
Parous, never	133	145	1.00		110	125	1.00	
Cumulative years of oral contraceptive use								
Never used	149	146	1.00		146	155	1.00	
< 1.5	59	82	0.71	0.46-1.09	80	67	1.32	0.85-2.06
1.5 - 5	54	75	0.61	0.38-0.98	67	114	0.76	0.48-1.19
> 5	67	84	0.70	0.45-1.09	83	118	0.86	0.56-1.32
Menopausal status								
Premenopausal	131	154	1.00		116	186	1.00	
Postmenopausal	178	219	1.18	0.67-2.08	239	249	0.86	0.51-1.48
Surgical Unknown	21	14	1.80	0.85-3.80	24	21	1.43	0.74-2.78

Table 1. (Continued)

Risk Factor	Hispanic				non-Hispanic White			
	Cases (n=332) No. †	Controls (n=388) No.	OR	95%CI	Cases (n=380) No.	Controls (n=456) No.	OR	95%CI
History of fibrocystic disease								
No	287	348	1.00		285	379	1.00	
Yes	45	40	1.31	0.83-2.09	95	77	1.68	1.18-2.39
Breast cancer in mother, sister, daughter								
No	292	352	1.00		317	402	1.00	
Yes	40	36	1.30	0.80-2.12	63	54	1.46	0.98-2.18
Cigarette smoking								
No	187	202	1.00		195	216	1.00	
Yes	145	186	0.84	0.62-1.14	185	240	0.84	0.63-1.11
Body mass index (kg/m^2) ‡								
< 21.1	35	75	1.00		119	134	1.00	
21.1 - <23.0	65	73	1.88	1.11-3.20	126	132	1.05	0.73-1.50
23.0 - <25.6	95	109	1.87	1.14-3.06	68	103	0.65	0.43-0.97
>= 25.6	133	124	2.38	1.46-3.87	65	85	0.81	0.53-1.24
Vigorous physical activity (METS/ week) §								
None/non-vigorous	148	106	1.00		108	87	1.00	
Light, <13	92	110	0.62	0.42-0.90	95	142	0.55	0.37-0.81
Moderate, 13 - <35	47	76	0.45	0.29-0.71	104	118	0.73	0.49-1.08
Heavy , >= 35	45	96	0.34	0.22-0.54	73	109	0.55	0.36-0.84
Energy intake (kilocalories/day)								
< 1608	68	87	1.00		105	79	1.00	
1608 - <2018	59	58	1.27	0.78-2.07	86	108	0.60	0.39-0.90
2019 - <2436	72	71	1.37	0.86-2.20	68	95	0.54	0.35-0.84
2436 - <3032	56	79	0.95	0.59-1.53	59	87	0.52	0.33-0.82
>= 3032	71	84	1.08	0.68-1.71	59	82	0.55	0.35-0.87
Total fat intake (grams/day) ¶								
< 58	75	80	1.00		106	86	1.00	
58 - <75	64	62	1.09	0.68-1.76	89	104	0.67	0.44-1.01
75 - <96	63	78	0.86	0.54-1.37	67	88	0.66	0.42-1.02
96 - <123	57	82	0.79	0.49-1.26	53	84	0.53	0.34-0.85
>= 123	67	77	0.92	0.57-1.46	62	89	0.57	0.37-0.89

Table 1. (Continued)

* Conditional logistic regression models matched for age-group, health planning district and additionally adjusted for age.

† Numbers (No.) may not sum to total for all covariates because of missing data.

‡ kg/m^2, kilograms/meters squared.

§ METS, metabolic equivalents, based on expenditure of kilocalories/kilogram of weight/hour. Physical activities included: walking/hiking, running/jogging, exercise class, biking, dancing, lap swimming, tennis, squash/racquetball, calisthenics/rowing, bowling, golf, softball/baseball, basketball, volleyball, housework, and heavy outside work.

¶ Absolute intake.

TABLE 2. Odds ratios (OR) and 95% confidence intervals (CI) for age-adjusted models, and multivariate-adjusted full models for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

Alcohol Exposure Variable	Hispanic						non-Hispanic White					
	Cases	Controls	Age-adjusted *		Full †		Cases	Controls	Age-adjusted		Full	
	No.	No.	OR	95%CI	OR	95%CI	No.	No.	OR	95%CI	OR	95%CI
Recent alcohol intake (grams/week) ‡§¶												
Nondrinker #	212	236	1.00		1.00		189	188	1.00		1.00	
< 8	33	43	0.89	0.54-1.47	1.21	0.68-2.15	34	47	0.71	0.43-1.16	0.49	0.28-0.85
8 - <21 (1 drink)	28	38	0.77	0.45-1.32	1.00	0.54-1.85	33	57	0.57	0.35-0.93	0.46	0.27-0.79
21 - <42 (2 drinks)	22	29	0.80	0.44-1.47	0.75	0.37-1.53	31	54	0.60	0.36-0.99	0.44	0.25-0.77
42 - <85 (3-4 drinks)	13	15	0.95	0.43-2.06	1.24	0.52-2.93	35	49	0.71	0.43-1.16	0.60	0.35-1.05
85 - <148 (5-7 drinks)	18	18	1.14	0.56-2.29	1.35	0.63-2.93	17	29	0.58	0.30-1.12	0.49	0.24-1.00
>= 148 (8+ drinks)	0	0					38	27	1.42	0.82-2.46	1.56	0.85-2.86

* Conditional logistic regression models matched for age-group and health planning district, and adjusted additionally for age.

† Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

‡ Absolute intake.

§ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

¶ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.

No intake in four-week period, six months in past.

TABLE 3. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with recent alcohol intake, collapsed into fewer categories, based on a food frequency questionnaire, stratified by ethnicity and menopausal status, New Mexico Women's Health Study, 1992-1994 *

	Hispanic - Recent Alcohol Intake †					
	Low		Medium		High	
	OR	95%CI	OR	95%CI	OR	95%CI
Nondrinker	1.00		1.00		1.00	
All §	1.21	0.68-2.15	0.88	0.54-1.45	1.31	0.72-2.38
Premenopausal	1.69	0.67-4.30	0.70	0.32-1.51	0.96	0.36-2.60
Postmenopausal	0.89	0.37-2.14	0.96	0.42-2.18	2.03	0.81-5.09

	non-Hispanic White - Recent Alcohol Intake ‡			
	Low		High	
	OR	95%CI	OR	95%CI
Nondrinker	1.00		1.00	
All §	0.49	0.35-0.69	1.55	0.84-2.83
Premenopausal	0.29	0.15-0.56	1.08	0.32-3.64
Postmenopausal	0.56	0.35-0.90	2.23	0.99-5.03

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Hispanic, levels of recent alcohol intake (grams/week): Low=<8 (<1 drink); Medium=8-<42 (1-2 drinks); High=42+ (3+ drinks).

‡ non-Hispanic White, levels of recent alcohol intake (grams/week): Low=<148 (<8 drinks); High=148+ (8+ drinks).

§ Menopausal status included in these models.

TABLE 4. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity and joint estrogen/progesterone receptor status, New Mexico Women's Health Study, 1992-1994 *

	Controls	ER+PR+			ER-PR-		
Alcohol Exposure Variable	No. †	No.	OR	95%CI	No.	OR	95%CI
Hispanic							
Recent alcohol intake (grams/week) ‡							
Nondrinker	236	80	1.00		50	1.00	
< 8	43	10	0.83	0.35-1.98	9	1.04	0.39-2.79
8 - <42 (1-2 drinks)	67	20	0.97	0.49-1.91	7	0.39	0.14-1.08
>= 42 (3+ drinks)	33	18	1.78	0.86-3.68	9	1.43	0.55-3.74
non-Hispanic White							
Recent alcohol intake (grams/week) ‡							
Nondrinker	188	72	1.00		33	1.00	
< 148 (<8 drinks)	236	59	0.46	0.28-0.74	27	0.37	0.19-0.73
>= 148 (8+ drinks)	27	22	2.13	1.03-4.43	5	1.62	0.51-5.18

* Logistic regression models adjusted for matching variables (age-group, health planning district), and for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Recent alcohol intake data missing for 14 controls, 5 cases with ES+PR+ status breast cancer, and 4 cases with ES-PR- status breast cancer. The remaining cases were categorized as: ES+PR- (77), ES-PR+ (20); hormone-receptor determination not done (108); and either results borderline or unknown (77).

‡ Absolute intake.

TABLE 5. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with ever *vs.* never alcohol consumption and alcohol usage patterns, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994 *

Alcohol Exposure Variable	Hispanic				non-Hispanic White			
	Cases (n=332)	Controls (n=388)			Cases (n=380)	Controls (n=456)		
	No.	No.	OR	95%CI	No.	No.	OR	95%CI
History of alcohol consumption								
Never	83	82	1.00		51	46	1.00	
Ever	249	306	0.96	0.61-1.50	329	410	0.72	0.43-1.19
Status of alcohol consumption at interview								
Nondrinker	83	82	1.00		51	46	1.00	
Current drinker	166	230	0.84	0.52-1.36	233	328	0.60	0.36-1.01
Former drinker	83	76	1.21	0.71-2.05	96	82	1.09	0.61-1.95
Years since last alcohol consumption †								
Nondrinker	83	82	1.00		51	46	1.00	
Stopped within reference year	21	2	12.13	2.51-58.6	23	3	8.04	2.03-31.7
1	7	4	2.77	0.57-13.5	9	3	2.10	0.48-9.23
2-4	11	7	1.86	0.58-5.95	13	10	1.57	0.54-4.55
5-14	18	14	1.65	0.67-4.05	24	32	0.78	0.36-1.66
>= 15	25	48	0.53	0.27-1.03	27	34	0.64	0.30-1.34
Current drinker	166	230	0.90	0.56-1.46	233	328	0.62	0.37-1.05
Age (years) at first alcohol use								
Nondrinker	83	82	1.00		51	46	1.00	
<= 16	40	63	0.71	0.37-1.36	72	120	0.61	0.33-1.12
17 - 18	47	70	0.67	0.36-1.23	94	117	0.67	0.39-1.20
19 - 21	72	88	0.95	0.55-1.65	95	102	0.80	0.45-1.42
>= 22	90	85	1.21	0.72-2.03	68	71	0.73	0.40-1.32
Duration (years) of drinking ††								
Nondrinker	83	82	1.00		52	46	1.00	
< 10	20	32	0.82	0.39-1.70	16	21	0.69	0.29-1.64
10 - 39	201	224	1.06	0.66-1.73	230	286	0.80	0.47-1.36
>= 40	27	49	0.76	0.37-1.57	82	103	0.60	0.33-1.09

Table 5. (Continued)

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Age when alcohol consumption stopped was missing for 1 case and 1 control.

‡ Does not reflect actual duration of drinking; based on reported age at cessation or reference age minus first age of alcohol use.

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APPENDIX A

ADDITIONAL TABLES

TABLE A_1. Covariates with 10 percent or greater change-in-estimate (odds ratio) for recent alcohol intake, based on a food frequency questionnaire, and average lifetime intake based on ages 25, 35, and 50, New Mexico Women's Health Study, 1992-1994 *

Covariate	Alcohol Exposure Variable	Hispanic			non-Hispanic White		
		Menopausal Status			Menopausal Status		
		All	Pre †	Post †	All	Pre	Post
Education	Recent	19	36	61	-	-	12
	Average lifetime	16	49	10	-	-	15
Age (years) at menarche	Recent	-	-	-25	-	-	10
	Average lifetime	-	19	-	-	-	-
Age (years) at first full-term birth	Recent	11	24	-	-	-	-11
	Average lifetime	-	23	-12	-	17	13
Number of full-term births	Recent	-	-	44	-	-	-11
	Average lifetime	12	39	10	-	-16	-15
Cumulative months of lactation	Recent	-	28	-	-	-	-
	Average lifetime	-	-21	-	-	-	-14
Cumulative years oral contraceptive use	Recent	-	25	35	-	-	-
	Average lifetime	16	33	16	-	-10	14
History of fibrocystic disease	Recent	-	-10	-15	-	-	-
	Average lifetime	-	-16	-	-	-	-
Breast cancer in mother, sister, daughter	Recent	-	-	-32	-	-	-
	Average lifetime	-	11	-	-	-	-
Cigarette smoking	Recent	-	-	-	10	-	38
	Average lifetime	13	-	12	-	-	27
Body mass index (kg/m^2) ‡	Recent	13	-	20	-	-25	19
	Average lifetime	-13	-64	10	-	-19	-
Vigorous physical activity (METS/week) §	Recent	-10	25	36	-	-	19
	Average lifetime	-	28	-24	-	21	-

Table A_1. (Continued)

Covariate	Alcohol Exposure Variable	Hispanic			non-Hispanic White		
		Menopausal Status			Menopausal Status		
		All	Pre †	Post †	All	Pre	Post
Energy intake (kilocalories/week)	Recent	-	-	20	16	-	34
	Average lifetime	11	-	-	-	-	-
Energy-adjusted total fat (grams/week)	Recent	11	-	27	-	-	-
	Average lifetime	-	-21	-	-	-11	-

* Change in estimate (odds ratio) < 10 percent noted as '-'.

† Pre, premenopausal; Post, postmenopausal.

‡ kg/m^2, kilograms/meters squared.

§ METS, metabolic equivalents, based on expenditure of kilocalories/kilogram of weight/hour.

TABLE A_2. Odds ratios (OR) and 95% confidence intervals (CI) for reduced models for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994

Alcohol Exposure Variable	Hispanic Reduced Model * OR	Hispanic Reduced Model * 95%CI	non-Hispanic White Reduced Model † OR	non-Hispanic White Reduced Model † 95%CI
Recent alcohol intake (grams/week) ‡§¶				
Nondrinker #	1.00		1.00	
< 8	1.28	0.73-2.25	0.65	0.39-1.08
8 - <21 (1 drink)	1.01	0.54-1.86	0.49	0.30-0.82
21 - <42 (2 drinks)	0.81	0.40-1.63	0.56	0.34-0.95
42 - <85 (3-4 drinks)	1.22	0.52-2.85	0.72	0.43-1.20
85 - <148 (5-7 drinks)	1.24	0.58-2.66	0.65	0.33-1.26
>= 148 (8+ drinks)			1.65	0.93-2.92

* Conditional logistic regression models matched for age-group and health planning district, and adjusted for all variables except for fibrocystic disease and cigarette smoking.

† Conditional logistic regression models matched for age-group and health planning district, and adjusted for age, energy intake, cigarette smoking, and body mass index.

‡ Absolute intake.

§ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

¶ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.

No intake in four-week period, six months in past.

TABLE A_3. Odds ratios (OR) and 95% confidence intervals (CI) for age-adjusted models, multivariate-adjusted full models and reduced models for breast cancer risk associated with recent alcohol intake, based on a food frequency questionnaire, stratified by ethnicity and menopausal status, New Mexico Women's Health Study, 1992-1994 *

	Premenopausal Status											
	Hispanic						non-Hispanic White					
Alcohol Exposure Variable	Age-adjusted *		Full †		Reduced ‡		Age-adjusted *		Full †		Reduced §	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Recent alcohol intake (grams/week) ¶#**												
Nondrinker ‡‡	1.00		1.00		1.00		1.00		1.00		1.00	
< 8	1.21	0.57-2.58	1.68	0.66-4.26	1.71	0.68-4.32	0.66	0.27-1.62	0.29	0.10-0.87	0.54	0.21-1.38
8 - <21 (1 drink)	0.73	0.33-1.61	0.64	0.24-1.71	0.64	0.24-1.72	0.33	0.15-0.71	0.24	0.09-0.61	0.30	0.13-0.67
21 - <42 (2 drinks)	1.02	0.44-2.35	0.78	0.26-2.32	0.81	0.28-2.31	0.48	0.23-1.02	0.28	0.11-0.75	0.43	0.19-0.95
42 - <85 (3-4 drinks)	1.28	0.43-3.82	1.68	0.43-6.47	1.76	0.48-6.48	0.60	0.26-1.38	0.40	0.14-1.14	0.59	0.25-1.41
85 - <148 (5-7 drinks)	0.65	0.22-1.86	0.61	0.16-2.25	0.54	0.15-1.96	0.58	0.18-1.88	0.29	0.07-1.17	0.64	0.19-2.15
>= 148 (8+ drinks)							1.24	0.45-3.43	1.08	0.32-3.68	1.04	0.36-3.02
	Postmenopausal Status											
Recent alcohol intake (grams/week) ¶#**												
Nondrinker ‡‡	1.00		1.00		1.00		1.00		1.00		1.00	
< 8	0.69	0.34-1.40	0.93	0.38-2.26	0.93	0.39-2.22	0.67	0.35-1.27	0.59	0.28-1.22	0.64	0.33-1.24
8 - <21 (1 drink)	0.83	0.36-1.87	1.47	0.55-3.92	1.54	0.58-4.09	0.92	0.46-1.83	0.63	0.29-1.37	0.72	0.35-1.48
21 - <42 (2 drinks)	0.49	0.17-1.42	0.43	0.12-1.62	0.52	0.14-1.93	0.45	0.20-1.01	0.36	0.15-0.92	0.42	0.18-0.97
42 - <85 (3-4 drinks)	0.65	0.18-2.33	0.83	0.21-3.35	0.73	0.18-2.93	0.81	0.42-1.55	0.67	0.31-1.44	0.85	0.43-1.66
85 - <148 (5-7 drinks)	2.54	0.89-7.27	4.25	1.18-15.3	4.23	1.15-15.6	0.61	0.28-1.33	0.54	0.22-1.34	0.73	0.32-1.62
>= 148 (8+ drinks)							1.53	0.76-3.09	2.23	0.98-5.05	2.17	1.03-4.58

Table A_3. (Continued)

* Conditional logistic regression models matched for age-group and health planning district, and adjusted additionally for age.

† Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

‡ Conditional logistic regression models matched for age-group and health planning district, and adjusted for all variables except for fibrocystic disease and cigarette smoking.

§ Conditional logistic regression models matched for age-group and health planning district, and adjusted for age, energy intake, cigarette smoking, and body mass index.

¶ Absolute intake.

\# Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

** Recent alcohol intake data missing or excluded for 9 cases and 14 controls.

‡‡ No intake in four-week period, six months in past.

TABLE A_4. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk associated with past alcohol intake at previous ages 25, 35, and 50, and average lifetime alcohol intake based on ages 25 through 50, stratified by ethnicity, New Mexico Women's Health Study, 1992-1994 *

Alcohol Exposure Variable	Hispanic				non-Hispanic White			
	Cases (n=332)	Controls (n=388)			Cases (n=380)	Controls (n=456)		
	No.	No.	OR	95%CI	No.	No.	OR	95%CI
Age 25, alcohol intake (grams/week) †‡§								
Nondrinker	83	82	1.00		51	46	1.00	
< 8	107	130	1.11	0.67-1.86	112	126	0.86	0.50-1.50
8 - <21 (1 drink)	28	33	0.86	0.42-1.73	45	48	0.70	0.36-1.37
21 - <42 (2 drinks)	17	23	0.97	0.42-2.26	32	37	0.70	0.34-1.44
42 - <85 (3-4 drinks)	18	20	1.12	0.48-2.64	38	58	0.58	0.30-1.12
85 - <148 (5-7 drinks)	16	23	0.68	0.28-1.66	25	32	0.73	0.34-1.58
>= 148 (8+ drinks)					16	33	0.41	0.18-0.96
Drank at other times	63	77	0.84	0.49-1.46	61	76	0.66	0.36-1.20
Age 35, alcohol intake (grams/week) †‡§¶								
Nondrinker	83	79	1.00		50	45	1.00	
< 8	101	113	1.12	0.66-1.89	102	116	0.77	0.44-1.36
8 - <21 (1 drink)	28	36	0.80	0.39-1.64	45	50	0.68	0.34-1.34
21 - <42 (2 drinks)	17	27	0.74	0.33-1.63	29	37	0.64	0.31-1.34
42 - <85 (3-4 drinks)	27	18	2.09	0.89-4.92	35	64	0.47	0.23-0.93
85 - <148 (5-7 drinks)	15	24	0.54	0.22-1.32	32	18	1.54	0.69-3.41
>= 148 (8+ drinks)					27	30	0.88	0.40-1.93
Drank at other times	46	64	0.78	0.43-1.41	51	66	0.67	0.36-1.26
Unexposed, reference age <35	15	27			9	30		
Age 50, alcohol intake (grams/week) †‡§¶								
Nondrinker	59	60	1.00		44	33	1.00	
< 8	51	47	1.08	0.52-2.26	59	50	0.88	0.44-1.74
8 - <21 (1 drink)	16	26	0.40	0.15-1.05	23	33	0.45	0.20-1.04
21 - <42 (2 drinks)	9	14	0.69	0.23-2.04	21	16	0.96	0.38-2.40
42 - <85 (3-4 drinks)	7	10	0.57	0.17-1.91	22	37	0.37	0.16-0.85
85 - <148 (5-7 drinks)	10	5	2.06	0.50-8.61	22	15	1.08	0.42-2.77
>= 148 (8+ drinks)					23	20	1.14	0.46-2.80
Drank at other times	33	47	0.61	0.29-1.31	47	36	1.01	0.48-2.11
Unexposed, reference age <50	147	179			119	216		

Table A_4. (Continued)

Alcohol Exposure Variable	Hispanic				non-Hispanic White			
	Cases (n=332)	Controls (n=388)			Cases (n=380)	Controls (n=456)		
	No.	No.	OR	95%CI	No.	No.	OR	95%CI
Average lifetime intake, ages 25 to 50 (grams/week) †‡§								
Nondrinker	83	82	1.00		51	46	1.00	
< 8	131	157	1.08	0.66-1.76	116	132	0.86	0.50-1.48
8 - <21 (1 drink)	31	37	0.90	0.46-1.78	50	63	0.56	0.29-1.07
21 - <42 (2 drinks)	32	40	0.96	0.49-1.88	36	58	0.53	0.27-1.04
42 - <85 (3-4 drinks)	19	23	1.23	0.53-2.81	57	70	0.70	0.38-1.32
85 - <148 (5-7 drinks)	23	28	0.67	0.30-1.48	32	29	0.76	0.36-1.60
>= 148 (8+ drinks)					27	39	0.70	0.33-1.47
Drank at other times	13	21	0.59	0.25-1.41	11	19	0.64	0.25-1.64

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for age, education, age at menarche, menopausal status, age at first full-term birth, number of full-term births, cumulative months of lactation, cumulative years of oral contraceptive use, history of fibrocystic disease, breast cancer in mother, sister, daughter, cigarette smoking, body mass index, physical activity, energy intake, and energy-adjusted total fat intake.

† Alcohol intake in grams categorized as in analyses of 'recent' alcohol intake.

‡ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.

§ The categories, former drinkers, drank at later ages, and current drinkers, but no data reported, were combined into 'drank at other times' because of small sample size and minimal change in estimates.

¶ Number of subjects at ages 35 and 50 based on total number of women whose reference age was equal to or greater than the age at alcohol intake (age 35 or age 50).

TABLE A_5. Selected characteristics of cases, stratified by status of alcohol consumption at diagnosis (n=712), New Mexico Women's Health Study, 1992-1994

	Cases			
	Non-Drinkers	Current Drinkers	Former Drinkers	
			Stop 1+ years prior to diagnosis age	Stop within year of diagnosis age
Characteristic	(n=134)	(n=399)	(n=135)	(n=44)
Ethnicity				
Hispanic (%)	62	42	46	48
Non-Hispanic White (%)	38	58	54	52
Education, >12 years (%)	25	59	43	52
Age *[1]	58±11	52±11	55±11	48±10
Energy intake, kilocalories/day	2287±1003	2303±912	2171±856	2330±961
Total fat intake, grams/day ‡	87±44	89±42	83±41	95±50
Body mass index (kg/m^2)	26±5	23±4	25±6	24±4
Cigarette smoking (%)	26	53	49	39
History of fibrocystic disease(%)	14	22	20	18
Oral contraceptive use (%)*[2]	43	66	47	73
Breast cancer in mother, sister, daughter (%)	17	15	11	9
Vigorous physical activity, >35 METS(%)	16	17	14	20
Premenopausal status (%)*[3]	17	40	30	57
Stage, regional or remote (%)*[4]	35	27	30	58
Age at first use of alcohol		21±8	22±7	20±5
Duration of drinking (years) *[5]		31±11	21±12	28±10
Age 25, alcohol intake (drinks/week)		2.7±4.8 (330) †	2.5±5.8 (88)	2.0±2.6 (36)
Age 35, alcohol intake (drinks/week) ‡		3.4±6.2 (343)	2.9±5.5 (78)	2.3±2.4 (37)
Age 50, alcohol intake (drinks/week) ‡		3.9±6.5 (219)	4.1±8.03 (32)	2.9±2.6 (13)
Lifetime average intake (drinks/week)		3.1±5.2 (391)	2.5±5.0 (119)	2.1±2.4 (44)

Table A_5. (Continued)

* Comparison of the two former drinker groups, $p<0.01$:

1 $F = 14.4$, $p=0.0002$
2 $\chi^2 = 9.0$, $p=0.003$
3 $\chi^2 = 16.5$, $p=0.000$
4 $\chi^2 = 10.8$, $p=0.001$
5 $F = 14.2$, $p=0.0002$

† Number shown in parentheses equal to number of women who reported drinking at specific ages (25, 35, 50). The lifetime average intake does not always equal the total for each group, because 11 women reported alcohol intake between the age intervals for which data was collected, and 13 women stopped drinking before the age of 25.

‡ Numbers of subjects at age 35 and 50, based on total number of women whose reference age was equal to or greater than the age at alcohol intake (age 35 or age 50).

APPENDIX II

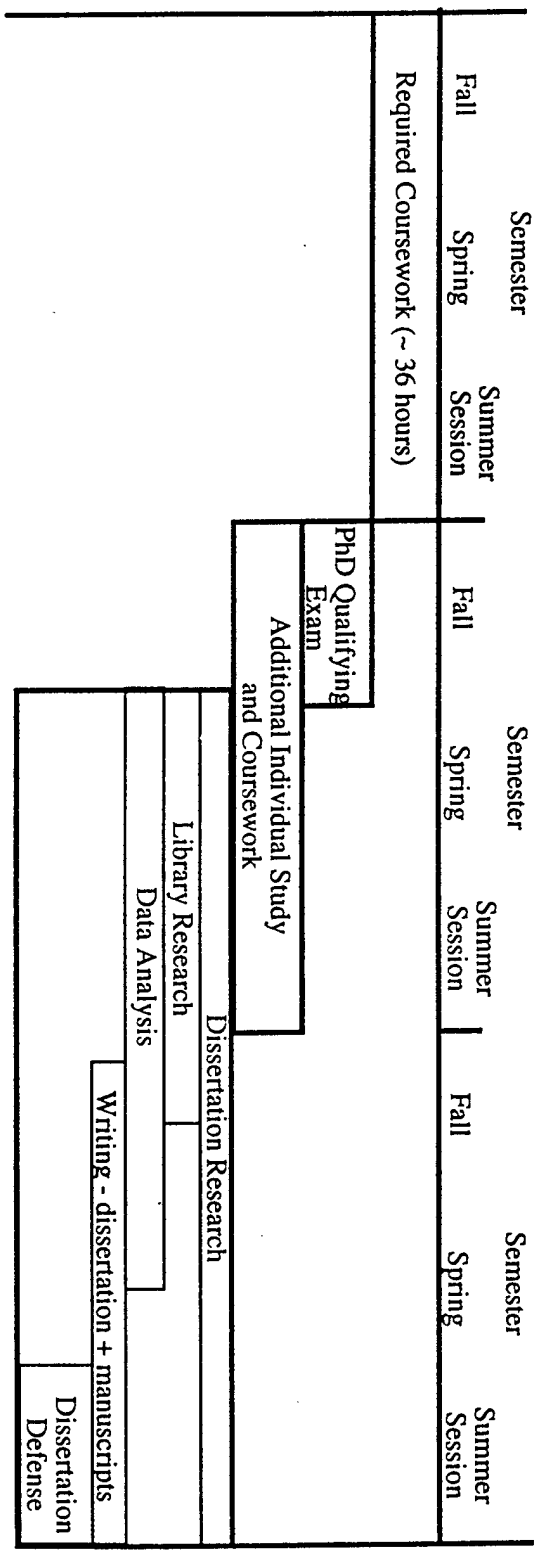
- Statement of Work

(from USAMRMC original 'Predoctoral Fellowship Application')

- Timeline

(from USAMRMC original 'Predoctoral Fellowship Application')

Timeline for Predoctoral Fellowship Application



Part 1. D. STATEMENT OF WORK

It is neither possible nor desirable to produce a structured statement of tasks to be accomplished during defined time periods for the proposed coursework and dissertation research, since progress is controlled to a large extent by the faculty and administration of the supporting educational institution. The time-line shown on the next page has been provided as a general guide, rather than a structured statement of work.

The time-line essentially divides the 3 year fellowship request into four critical time-blocks in which specific objectives are to be met.

Time-Block 1: This block represents the required year of coursework for qualification for the doctoral degree at the University of Texas School of Public Health. A minimum of 36 hours of coursework are required before approval to take the doctoral qualifying examination. The following is a tentative list of courses available at UTSPH that may be taken.

Proposed Coursework: University of Texas School of Public Health (UTSPH) Courses by Call Number (see 1993-1995 Catalog)

1996 (12 courses, 36 credit hours minimum required prior to Doctoral Qualifying Examination)

PH 1820 Applied Statistical Analysis I
PH 1821 Applied Statistical Analysis II
PH 1830 Advanced Statistical Methods in Epidemiology
PH 1831 Analysis of Survival Time Data
PH 2165 Mutagenesis and Carcinogenesis
PH 2175 Principles of Toxicology
PH 2712 Advanced Epidemiologic Methods III
PH 6215 Nutritional Epidemiology
PH 2998 Special Topics in Epidemiology - Cancer Epidemiology
2 x PH 2999 Individual Study in Epidemiology

1997 (number of courses optional)

PH 9999 Dissertation Research
PH 2999 Individual Study in Epidemiology

1998 (number of courses optional)

PH 9999 Dissertation Research
PH 2999 Individual Study in Epidemiology

Time-Block 2: This block represents the PhD qualifying exam which may be taken sometime during the Summer or Fall, at earliest, subsequent to completion of the proposed coursework.

Time-Block 3: The third block represents an additional year of advanced, individual study and special coursework (e.g. molecular biology and genetics) not offered at the UT School of Public Health, but at nearby institutions (e.g. Graduate School of Biomedical Sciences). This block will overlap with the fourth, which will include the initiation of library research and analysis of data from the NMWHS.

Time-Block 4: The goals of the fourth block will be to complete the dissertation, including the dissertation defense, as well as a report or published article by the end of the third year of the fellowship.

APPENDIX III

- Letter Regarding Candidacy for Doctoral Degree
- List of Completed Courses
- Approval of Doctoral Thesis Committee
- UTSPH Notice of Approval to Begin Research
- UTSPH Copy of Diploma

THE UNIVERSITY OF TEXAS
HOUSTON
HEALTH SCIENCE CENTER

School of Public Health
Office of the Dean

September 19, 1997

Kathy Baumgartner
School of Public Health
Student Mail Box

Dear Dr. Baumgartner,

Congratulations on the successful completion of your qualifying examination for the PhD degree which officially converts you from a doctoral student to a doctoral candidate.

We are pleased to have the opportunity to continue working with you as you proceed toward completion and presentation of an original research project that makes a substantial contribution to knowledge in community health sciences.

Yours sincerely,

R. Palmer Beasley, M.D.
Dean

for RPB: fg
cc: Student Records
file/comp

UT Houston School of Public Health • P.O. Box 20186 • Houston, Texas 77225 • (713) 500-9050 FAX (713) 500-9070

List of Completed Courses

1996
Applied Statistical Analysis (4)
Advanced Statistical Methods in Epidemiology - Logistic Regression (2)
Analysis of Survival Time Data (2)
Principles of Toxicology I (3)
Topics in Cancer Prevention I (1)
12 credit hours

1997
Advanced Epidemiologic Methods II (4)
Toxicology - Toxic Agents (3)
Pathology and Public Health (3)
Genetic Epidemiology (2)
Regression and Logistic Regression Analysis (4)
The Biology and Epidemiology of Cancer (2)
Molecular Epidemiology (2)
Breast Cancer: Diet and Alcohol (4)
Dissertation Research (1)
24 credit hours

1998
Dissertation Research (3)
Epidemiologic Design and Analysis(2)
Causal Inference (1)
6 credit hours

1999
Dissertation Research (1)

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT HOUSTON

SCHOOL OF PUBLIC HEALTH

REVISED 3-27-98 COPY

REQUEST TO **APPOINT A Ph.D. DOCTORAL THESIS COMMITTEE**
TO BE SUBMITTED BY STUDENT'S ADVISOR

DATE 2/9/98

STUDENT'S NAME Kathy B. Baumgartner EPI

I SHOULD LIKE TO REQUEST THAT THE FOLLOWING FACULTY BE APPOINTED TO THIS STUDENT'S DOCTORAL THESIS COMMITTEE.

EPI/HSO
J. F. Annegers — FACULTY — Epi — MAJOR F

EPI/HP
R. Sue McPherson — FACULTY — Epid — MAJOR F

Biom/HP/OccH
Ralph Frankowski — FACULTY — Biometry — MINOR FIELD

Health MSurf — Epidemiology — Field

I REQUEST THAT J. Fred Annegers CHAIR THE COMMITTEE.

John F. Annegers
ADVISOR

JOHNS HOPKINS UNIVERSITY

Jonathan M. Samet, M.D., M.S.
Professor and Chairman

Department of Epidemiology
School of Hygiene and Public Health
615 North Wolfe Street / Suite W6041
Baltimore MD 21205-2179
Office (410) 955-3286 / FAX (410) 955-[illegible]
Home (410) 539-8982 / Pager (800) 359-[illegible]
internet:jsamet@jhsph.edu

☑ REQUEST APPROVED

☐ REQUEST COULD NOT BE APPROVED BECAUSE _____

DEAN Blair Justice DATE 4-17-98

DISTRIBUTION CODE:

WHITE COPY — **Student File**
BLUE COPY — **Advisor**
GREEN, YELLOW & PINK COPIES — **Faculty Members**
GOLDENROD COPY — **Student**

THE UNIVERSITY OF TEXAS
HOUSTON
HEALTH SCIENCE CENTER

The Committee for the
Protection of Human Subjects

NOTICE OF APPROVAL TO BEGIN RESEARCH January 16, 1998

HSC-SPH-98-007 - "Alcohol Consumption and Breast Cancer Among Hispanic and Non-Hispanic White Women in New Mexico"
PI: Kathy Baumgartner, PhD Student; Chair - Dr. Annegers

PROVISIONS: Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consents, etc.

APPROVED: At a Convened Meeting

APPROVAL DATE: January 16, 1998 **EXPIRATION DATE:** December 31, 1998

CHAIRPERSON: Anne Dougherty, MD

Subject to any provisions noted above, you may now begin this research.

CHANGES - The P.I. must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.

INFORMED CONSENT - Informed consent must be obtained by the P.I. or designee using the format and procedures approved by the CPHS. The P.I. must instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document.

UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS - The P.I. will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious harm to subjects, and of any adverse drug reactions.

RECORDS - The P.I. will maintain adequate records, including signed consent documents if required, in a manner which ensures confidentiality.

1996[illegible] O.700 John Freeman Building • P.O. Box 20036 • Houston, Texas 77225 • (713) 500-3827 FAX (713) 500-3830
sboone@oac.hsc.uth.tmc.edu
Located in the Texas Medical Center

The University of Texas
Health Science Center at Houston
School of Public Health

Be it known that

Kathy B Baumgartner

having completed the prescribed course of study has been admitted to the degree of

Doctor of Philosophy

with all the rights, privileges, and responsibilities pertaining to that degree
Issued by the Board of Regents upon recommendation of the Faculty

Witness the seal of the University and the signatures the seventh day of May, A. D., nineteen hundred and ninety-nine.

Chairman, Board of Regents

Chancellor, The University of Texas System

President

Dean

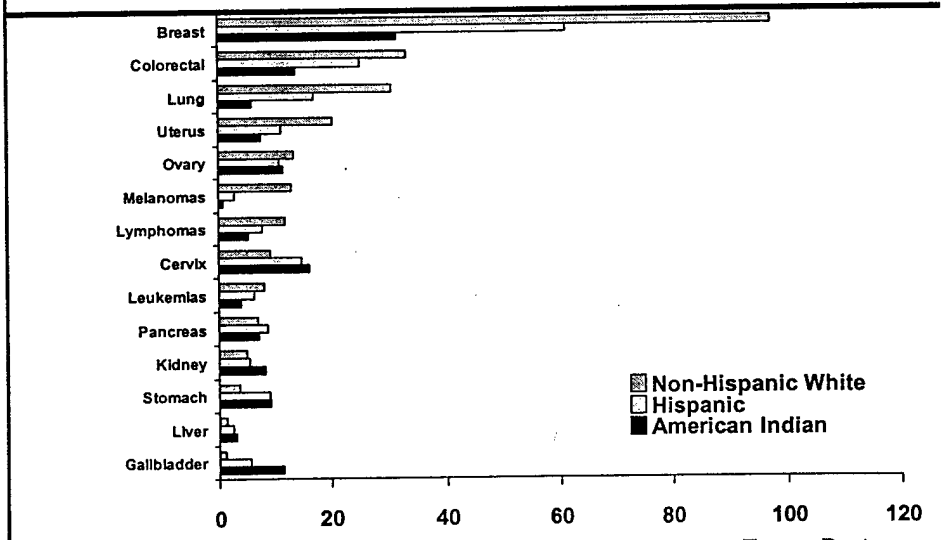
APPENDIX IV

Doctoral Presentation

ALCOHOL CONSUMPTION AND BREAST CANCER RISK AMONG HISPANIC AND non-HISPANIC WHITE WOMEN IN NEW MEXICO

Kathy B. Baumgartner

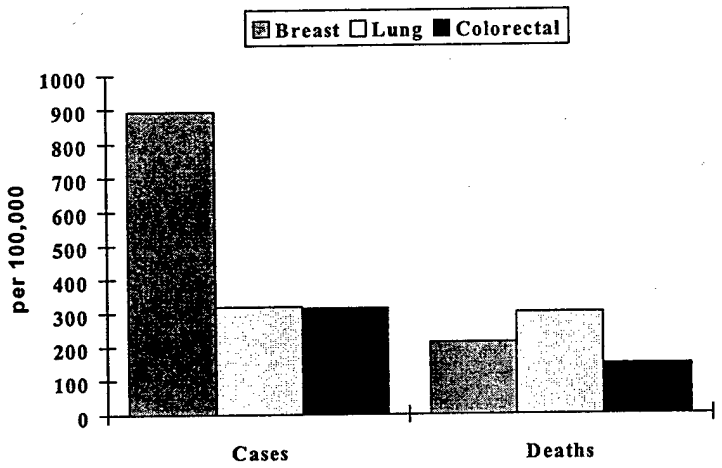
Cancer Incidence Rates* - Most Common Sites New Mexico Females, 1969-1997



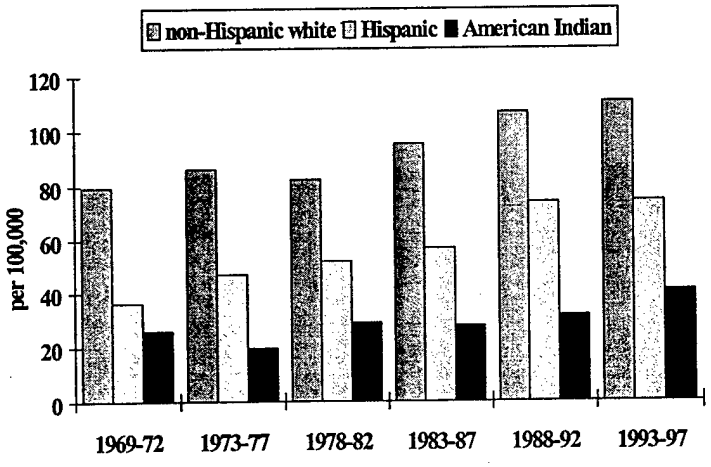
*Age-adjusted rates per 100,000

New Mexico Tumor Registry

Leading Cancers in New Mexico Females, 1997

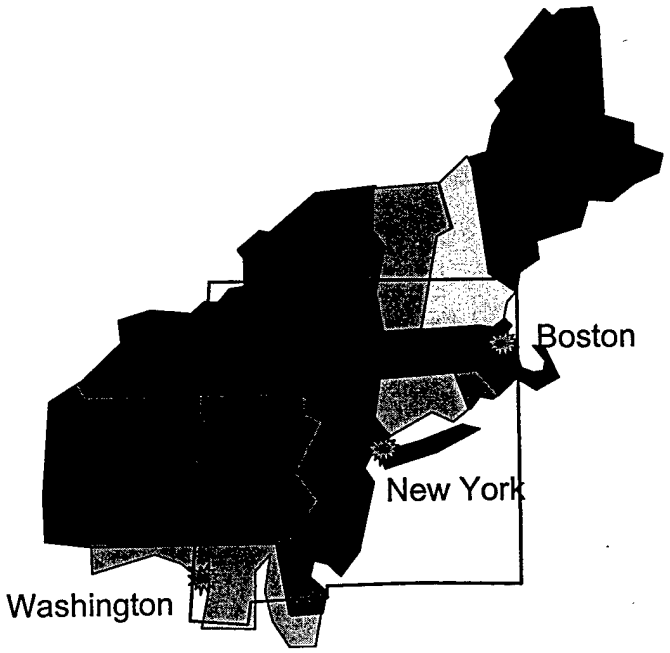


Breast Cancer Incidence Rates New Mexico Females, 1969-1997



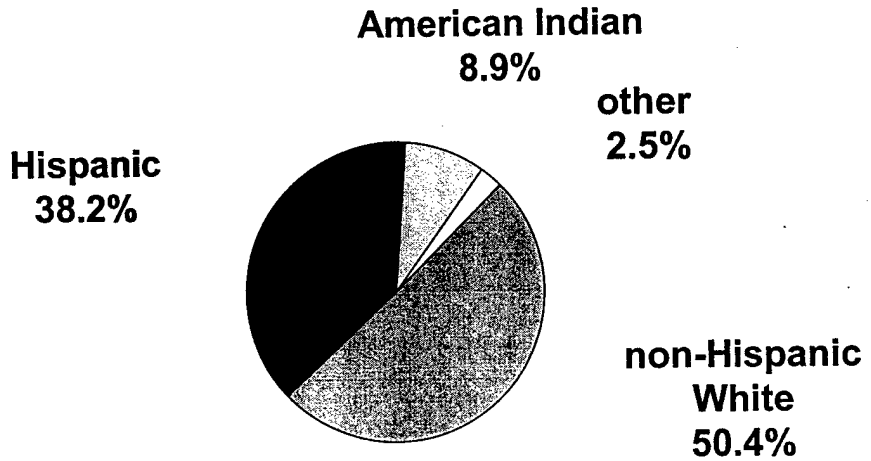
New Mexico

- 5th largest state
- Encompasses 121,600 square miles
- Population 1,515,069

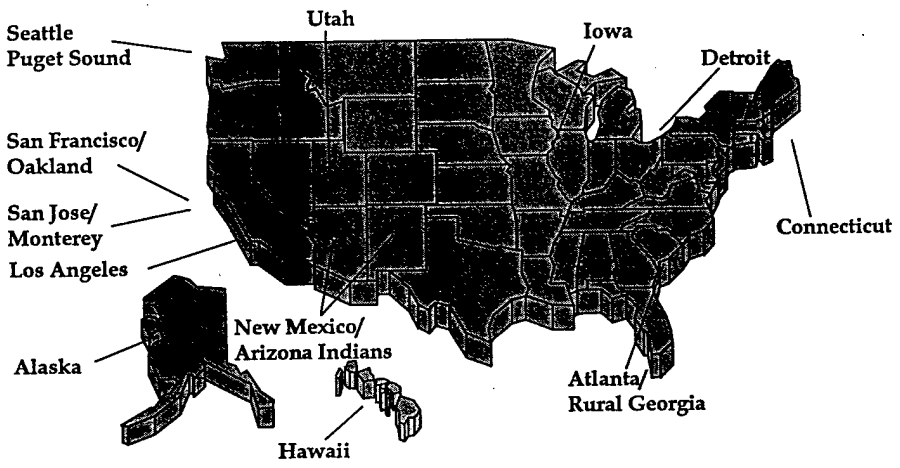


New Mexico's Population

1990 U.S. Census



Surveillance, Epidemiology, and End Results Program (SEER) National Cancer Institute



New Mexico Women's Health Study

- **Design**
  - » Statewide population-based case-control study initiated in 1992
- **Purpose**
  - » Investigate etiologic risk factors for breast cancer among Hispanic and non-Hispanic white women

Study Questions
Investigated by Menopausal Status

Alcohol consumption associated with:

- Increased breast cancer risk among Hispanic and non-Hispanic white women;
- Higher risk in Hispanics compared with non-Hispanic whites; and,
- Increased risk for hormone-receptor negative breast cancer.

Subject Recruitment - Cases

- Incident breast cancer cases
- Ascertained through the New Mexico Tumor Registry
- Eligibility
  - » Age 30 - 74 years
  - » Diagnosis between January 1992 and December 1994
  - » New Mexico residency at time of diagnosis
- All Hispanic cases included
- Random selection of ~ 33% non-Hispanic White cases
  - » Age-group (30-39, 40-64, 65-74 years)
  - » Geographic region (7 health planning districts)

Subject Recruitment - Controls

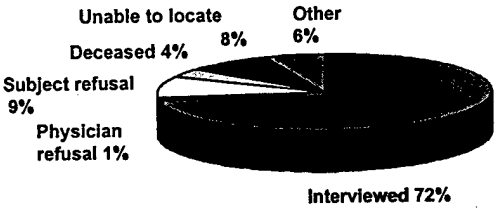
- **Recruitment**
  - » Waksberg random digit-dialing method
- **Frequency match on:**
  - » Ethnicity
  - » Age-group (30-39, 40-64, 65-74 years)
  - » Geographic region (7 health planning districts)

Data Collection
In-Home Interview

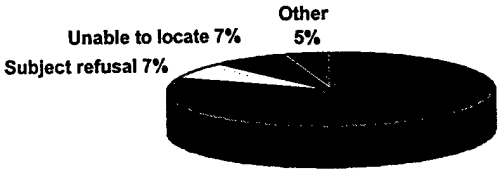
- **Food Frequency Questionnaire (FFQ)**
  - » 'Usual' food intake for 4-week period, 6 months prior to interview
    - » Recent alcohol intake (wine, beer, hard-liqour)
- **Risk Factor Questionnaire (RFQ)**
  - » Demographic chacteristics and breast cancer risk factors
    - » Past alcohol intake (wine, beer, hard-liqour)
    - » ever *vs.* never
    - » age at first use
    - » age at cessation
    - » frequency and number of drinks at ages 25, 35, 50
    - » lifetime (based on average intake at ages 25, 35, 50

Case Ascertainment *vs.* Control Recruitment

Cases H 491
NHW 493



Controls H 511
NHW 528



Other = moved out of state, interview incomplete, and for controls, not interviewed because control quota was filled

Statistical Analysis *

- **Conditional logistic regression** (matched design)
  - » age-adjusted
  - » multivariate-adjusted for covariates
- **Polytomous logistic regression**
  - » joint classification of hormone receptors (ES+PR+, ES-PR-) relative to controls

* Computed using STATA

Results

	Hispanic		non-Hispanic White	
	Cases	Controls	Cases	Controls
Interviewed Subjects(n)	332	388	380	456
Mean Age *	52.5	52.4	54.7	52.5
Past Alcohol Intake(%)	75	79	87	90
Recent Alcohol Intake(%)	34	37	49	58

* age at diagnosis for cases, age at interview for controls

Percent Distribution of Covariates Stratified by Ethnicity and Case-Control Status

	HISPANIC		non-HISPANIC WHITE	
Risk Factor	Cases (n=332)	Controls (n=388)	Cases (n=380)	Controls (n=456)
Education, > 12 y	29	39	67	69
Age at menarche, <=12 y	40	44	49	46
Age at first full-term birth, >22 y	35	31	49	47
Number of full-term births				
Nulliparous	11	8	16	16
1 - 3	53	53	67	65
> 4	36	39	17	19
Cumulative months of lactation				
Parous 1 - 12	33	33	44	34
Parous > 12	16	21	11	22
Parous Never	40	38	29	28
Cumulative years of OC use, >=5 y	20	22	22	26

Percent Distribution of Covariates Stratified by Ethnicity and Case-Control Status

	HISPANIC		non-HISPANIC WHITE	
	Cases (n=332)	Controls (n=388)	Cases (n=380)	Controls (n=456)
Menopausal status *				
Premenopausal	39	40	31	41
Postmenopausal status	54	56	63	55
History of fibrocystic disease	14	10	25	17
Breast cancer, mother,sister,daughter	12	9	17	12
Cigarette smoking	44	48	49	53
Body mass index >= 25.6 kg/m^2	40	32	17	19
Physical activity >= 35 METS/week	14	25	19	24
Energy intake >= 2436 kilocalories/day	37	42	31	37
Total fat intake >= 96 grams/day	37	41	30	38

* 5% of women could not be classified as pre- or postmenopausal

Age-Adjusted ORs and 95% CIs for Breast Cancer Risk Associated with Recent Alcohol Intake, based on FFQ *

	HISPANIC				non-HISPANIC WHITE			
Recent Alcohol Intake (grams/week) †‡§	Cases No.	Controls No.	OR	95%CI	Cases No.	Controls No.	OR	95%CI
Nondrinker ¶	212	236	1.0		189	188	1.0	
< 8	33	43	0.9	0.5-1.5	34	47	0.7	0.4-1.2
8 - <21 (1 drink)	28	38	0.8	0.5-1.3	33	57	0.6	0.4-0.9
21 - <42 (2 drinks)	22	29	0.8	0.4-1.5	31	54	0.6	0.4-1.0
42 - <85 (3-4 drinks)	13	15	1.0	0.4-2.1	35	49	0.7	0.4-1.2
85 - <148 (5-7 drinks)	18	18	1.1	0.6-2.3	17	29	0.6	0.3-1.1
>= 148 (8+ drinks)					38	27	1.4	0.8-2.5

* Conditional logistic regression models matched for age-group, health planning district and additionally adjusted for age.
† Absolute intake.
‡ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.
§ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.
¶ No intake in four-week period, six months in past.

Multivariate-Adjusted ORs and 95% CIs for Breast Cancer Risk Associated with Recent Alcohol Intake, based on FFQ *

	HISPANIC				non-HISPANIC WHITE			
Recent Alcohol Intake (grams/week) †‡§	Cases No.	Controls No.	OR	95%CI	Cases No.	Controls No.	OR	95%CI
Nondrinker ¶	212	236	1.0		189	188	1.00	
< 8	33	43	1.2	0.7-2.2	34	47	0.5	0.3-0.9
8 - <21 (1 drink)	28	38	1.0	0.5-1.9	33	57	0.5	0.3-0.8
21 - <42 (2 drinks)	22	29	0.8	0.4-1.5	31	54	0.4	0.3-0.8
42 - <85 (3-4 drinks)	13	15	1.2	0.5-2.9	35	49	0.6	0.4-1.1
85 - <148 (5-7 drinks)	18	18	1.4	0.6-2.9	17	29	0.5	0.2-1.0
>= 148 (8+ drinks)					38	27	1.6	0.9-2.9

* Conditional logistic regression models matched for age-group, health planning district, and adjusted for all covariates.
† Absolute intake.
‡ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.
§ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.
¶ No intake in four-week period, six months in past.

Covariates With >=10% Change in Odds Ratios, Compared with Full Model for Recent Alcohol Intake, based on FFQ *

	HISPANIC			non-HISPANIC WHITE		
	Menopausal Status			Menopausal Status		
	All	Pre †	Post †	All	Pre	Post
Education	19	36	61	-	-	12
Age (years) at menarche	-	-	-25	-	-	10
Age (years) at FFTB	11	24	-	-	-	-11
Number FFTB	-	-	44	-	-	-11
Cumulative months lactation	-	28	-	-	-	-
History fibrocystic disease	-	-10	-15	-	-	-
Cumulative years OC use	-	25	35	-	-	-
BMI (kg/m^2) ‡	13	-	20	-	-25	19
Cigarette smoking	-	-	-	10	-	38
Family history breast cancer	-	-	-32	-	-	-
Physical activity (METS/week) §	-10	25	36	-	-	19
Energy intake (kcals/week)	-	-	20	16	-	34
Energy-adjusted total fat (g/week)	-	-	27	-	-	-

* Change in estimate < 10 percent noted as '-'
† Pre, premenopausal; Post, postmenopausal
‡ kg/m^2, kilograms/meters squared
§ METS, metabolic equivalents, based on expenditure of kcals/kg per weight/hr

ORs and 95% CIs for Multivariate Reduced Models Recent Alcohol Intake - Stratified by Ethnicity

	Hispanic *		non-Hispanic White†	
	OR	95% CI	OR	95% CI
Nondrinker #	1.0		1.0	
< 8	1.3	0.7-2.3	0.7	0.4-1.1
8 - <21 (1 drink)	1.0	0.5-1.9	0.5	0.3-0.8
21 - <42 (2 drinks)	0.8	0.4-1.6	0.6	0.3-0.9
42 - <85 (3-4 drinks)	1.2	0.5-2.9	0.7	0.4-1.2
85 - <148 (5-7 drinks)	1.2	0.6-2.7	0.7	0.3-1.3
>= 148 (8+ drinks)			1.7	0.9-2.9

* Conditional logistic regression model matched for age-group and health planning district, and adjusted for all variables except for fibrocystic disease and cigarette smoking.
† Conditional logistic regression model matched for age-group and health planning district, and adjusted for age, energy intake, cigarette smoking, and body mass index.
‡ Absolute intake.
§ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.
¶ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.
# No intake in four-week period, six months in past.

ORs and 95% CIs for Multivariate Full and Reduced Models
Recent Alcohol Intake - Stratified by Ethnicity

	Hispanic *		non-Hispanic White†	
	Full	Reduced *	Full	Reduced †
Nondrinker #	1.00	1.00	1.00	1.00
< 8	1.21	1.28	0.49	0.65
8 - <21 (1 drink)	1.00	1.01	0.46	0.49
21 - <42 (2 drinks)	0.75	0.81	0.44	0.56
42 - <85 (3-4 drinks)	1.24	1.22	0.60	0.72
85 - <148 (5-7 drinks)	1.35	1.24	0.49	0.65
>= 148 (8+ drinks)			1.56	1.65

* Conditional logistic regression model matched for age-group and health planning district, and adjusted for all variables except for fibrocystic disease and cigarette smoking.
† Conditional logistic regression model matched for age-group and health planning district, and adjusted for age, energy intake, cigarette smoking, and body mass index.
‡ Absolute intake.
§ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.
¶ Recent alcohol intake data missing or excluded for 9 cases and 14 controls.
# No intake in four-week period, six months in past.

Recent Alcohol Intake (collapsed)
ORs and 95% CIs for Multivariate Full Models
Stratified by Ethnicity and Menopausal Status

HISPANIC *	LOW		MEDIUM		HIGH	
	OR	95%CI	OR	95%CI	OR	95%CI
All	1.2	0.7-2.2	0.9	0.5-1.5	1.3	0.7-2.4
Premenopausal	1.7	0.7-4.3	0.7	0.3-1.5	1.0	0.4-2.6
Postmenopausal	0.9	0.4-2.1	1.0	0.4-2.2	2.0	0.8-5.1

non-HISPANIC WHITE **	LOW		HIGH	
	OR	95%CI	OR	95%CI
All	0.5	0.4-0.7	1.6	0.8-2.8
Premenopausal	0.3	0.2-0.6	1.1	0.3-3.6
Postmenopausal	0.6	0.4-0.9	2.2	1.0-5.0

* Grams/week - Low=<8 (<1 drink); Medium=8 - <42 (1-2 drinks), High=42+ (3+ drinks)
** Grams/week - Low=<148 (<8 drinks); High=148+ (8+drinks)

Multivariate-Adjusted ORs and 95% CIs for Breast Cancer Risk Associated with Recent Alcohol Intake, based on FFQ, Stratified by Ethnicity and Joint Estrogen/Progesterone (ES/PR) Receptor Status *

Recent Alcohol Intake	Controls	ES+PR+			ES-PR-		
(grams/week) †	No.	No.	OR	95%CI	No.	OR	95%CI
HISPANIC							
Nondrinker	236	80	1.0		50	1.0	
< 8	43	10	0.8	0.4-2.0	9	1.0	0.4-2.8
8 - <42 (1-2 drinks)	67	20	1.0	0.5-1.9	7	0.4	0.1-1.1
>=42 (3+ drinks)	33	18	1.8	0.9-3.7	9	1.4	0.6-3.7
non-HISPANIC WHITE							
Nondrinker	188	72	1.0		33	1.0	
<148 (<8 drinks)	236	59	0.5	0.3-0.7	27	0.4	0.2-0.7
>= 148 (8+ drinks)	27	22	2.1	1.0-4.4	5	1.6	0.5-5.2

* Logistic regression models adjusted for matching variables (age-group, health planning district) and all covariates.
† Absolute intake.
‡ Recent alcohol intake missing for 14 controls, 5 cases ES+PR+, 4 cases ES-/PR-. Not included in analysis: ES+PR- (77), ES-PR+ (20), not done (108), results borderline or unknown (77).

Multivariate-Adjusted ORs and 95% CIs for Breast Cancer Risk Associated with Average Lifetime Alcohol Intake (Ages 25,35,50) *†

	HISPANIC				non-HISPANIC WHITE			
Average Lifetime Intake	Cases	Controls			Cases	Controls		
(age 25-50) (gs/week) ‡§	No.	No.	OR	95%CI	No.	No.	OR	95%CI
Nondrinker	83	82	1.0		51	46	1.0	
< 8	131	157	1.1	0.7-1.8	116	132	0.9	0.5-1.5
8 - <21 (1 drink)	31	37	0.9	0.5-1.8	50	63	0.6	0.3-1.1
21 - <42 (2 drinks)	32	40	1.0	0.5-1.9	36	58	0.5	0.3-1.0
42 - <85 (3-4 drinks)	19	23	1.2	0.5-2.8	57	70	0.7	0.4-1.3
85 - <148 (5-7 drinks)	23	28	0.7	0.3-1.5	32	29	0.8	0.4-1.6
>= 148 (8+ drinks)					27	39	0.7	0.3-1.5
Drank at other times	13	21	0.6	0.3-1.4	11	19	0.6	0.3-1.6

* Conditional logistic regression models matched for age-group, health planning district and adjusted for all other covariates.
† Alcohol intake in grams categorized as in analyses of 'recent' alcohol intake.
‡ Categories for 5-7 drinks and 8+ drinks combined for Hispanic women.
§ Categories, former drinkers, drank at later ages, and current drinkers, but no data reported, combined into 'drank at other times' due to small sample size and minimal change in estimates.

Summary - Findings

- No association with past alcohol intake
- Significant protective effect for light to moderate recent alcohol intake in non-Hispanic white women (pre- and postmenopausal)
- Suggestion for an increased risk at the highest level of recent alcohol intake among non-Hispanic white and postmenopausal Hispanic women
- Effects among non-Hispanic white women independent of hormone-receptor status

Summary - Conclusions

- Alcohol intake is not a risk factor for breast cancer in New Mexico Hispanic women
- Alcohol intake is not a strong risk factor for breast cancer in New Mexico non-Hispanic white women
- More studies needed to explain the mechanisms underlying either a protective effect or threshold for increased risk

Summary - Limitations

- Recall bias
- Information bias
- Confounding factors
- Multiple comparisons
- Unable to adequately evaluate high levels of alcohol intake

ACKNOWLEDGEMENTS

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